Modeling the diffusion magnetic resonance imaging signal inside neurons

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Abstract. The Bloch-Torrey partial differential equation (PDE) describes the complex transverse water proton magnetization due to diffusion-encoding magnetic field gradient pulses. The integral of the solution of this PDE yields the diffusion magnetic resonance imaging (dMRI) signal. In a complex medium such as cerebral tissue, it is difficult to explicitly link the dMRI signal to biological parameters such as the cellular geometry or the cellular volume fraction. Studying the dMRI signal arising from a single neuron can provide insight into how the geometrical structure of neurons influences the measured signal. We formulate the Bloch-Torrey PDE inside a single neuron, under no water exchange condition with the extracellular space, and show how to reduce the 3D simulation in the full neuron to a 3D simulation around the soma and 1D simulations in the neurites. We show that this latter approach is computationally much faster than full 3D simulation and still gives accurate results over a wide range of diffusion times.

1. Introduction

Diffusion magnetic resonance imaging (dMRI) is an imaging modality that gives a measure of the average displacement of water molecules in biological tissue during a diffusion time in the range of tens of milliseconds [1]. In a complex medium such as cerebral tissue, it is difficult to explicitly link the dMRI signal to biological parameters such as the cellular geometry or the cellular volume fraction. Studying the dMRI signal arising from a single neuron can provide insight into how the geometrical structure of neurons influences the measured signal.

Neurons are made of a neuronal body called the soma to which are attached long protrusions called neurites (axons and dendrites). The size of the soma is on the order
of 10 \mu m, the diameter of the dendrite segments can range from a few \mu m to less than half a \mu m, and the total length of all the dendrite segments is on the order of several mm \[2\]. The Bloch-Torrey partial differential equation (PDE) describes the complex transverse water proton magnetization due to diffusion-encoding magnetic field gradient pulses. The integral of the solution of this PDE yields the diffusion magnetic resonance imaging (dMRI) signal \[3, 4, 5\]. In a first step, we focus on the dMRI signal arising from the interior of a single neuron, without considering the water exchange between neurons and the extracellular space.

2. Theory

Let $\Omega \subset \mathbb{R}^3$ be the spatial domain that defines the geometry of a neuron. We denote the time profile of the diffusion-encoding magnetic field gradient by $f(t)$ and its linear spatial dependence by $G(r) = g \cdot r$, where the vector $g$ contains the amplitude and direction information of the magnetic field gradient. The water proton magnetization $M(r,t)$ satisfies the Bloch-Torrey PDE:

$$\frac{\partial}{\partial t} M(r,t) = -I \gamma f(t) G(r) M(r,t) + \nabla \cdot \left( D^0 \nabla M(r,t) \right), \quad r \in \Omega,$$

where $\gamma = 2.67513 \times 10^8 \text{rad s}^{-1}\text{T}^{-1}$ is the gyromagnetic ratio of the water proton, $I$ is the imaginary unit, and $D^0$ the intrinsic diffusion coefficient. The magnetization $M(r,t)$ is a function of position $r$ and time $t$, and depends on the diffusion gradient vector $g$ and the time profile $f(t)$. We will solve the Bloch-Torrey PDE for the Pulsed Gradient Spin Echo (PGSE) sequence \[6\], consisting of two rectangular pulses of duration $\delta$, separated by a time interval $\Delta - \delta$ (Fig. 1).

![Figure 1: The temporal profile $f(t)$ of a standard PGSE sequence with two rectangular gradient pulses.](image)

For the signal arising only from the neuron, without water exchange with the extracellular space, the boundary condition is:

$$\nabla M(r,t) \cdot n(r) = 0, \quad r \in \partial \Omega,$$

where $n(r)$ is the normal to the boundary $\partial \Omega$ at $r$. Assuming a uniform excitation of the magnetization in the imaging voxel, the initial condition is:

$$M(r,0) = 1.$$
The dMRI signal is measured at echo time $t = TE \geq \Delta + \delta$ and is given as the integral of $M(r, TE)$, normalized by the mass:

$$S^{3D}(b) := \frac{1}{|\Omega|} \int_{r \in \Omega} M(r, TE) \, dr,$$

where the $b$-value, $b(g) = \gamma^2 |g|^2 \delta^2 (\Delta - \delta/3)$, is used when $g$ varies only in amplitude (while staying in the same direction). In a homogeneous medium, the signal attenuation is simply $e^{-D_0 b}$.

The model described above will be called the full 3D model.

### 3. The 3D+1D model

We assume the neuron is made up of two sub-domains: the soma $S$ and the neurites $\mathcal{N}$, such that $\Omega = S \cup \mathcal{N}$. To simplify the presentation, we consider that the neurites attached to the soma are the union of straight cylinder segments: $\mathcal{N} = \bigcup_k \mathcal{B}_k$, where $\mathcal{B}_k = T_k \times O_k$, $T_k$ is a 1D line segment of length $l_k$, parallel to the unit vector $w_k$, and $O_k$ is the disk of radius $r$ perpendicular to $w_k$. Figure 2a shows an example of a neuron consisting of a spherical soma attached to two dendrite trees.

![Figure 2: Full 3D neuron (2a) and its 3D+1D model (2b).](image)

We now formulate an approximation of the full 3D model (Eqs. [1], [2]) where we replace the 3D PDE in the neurites by a 1D PDE on the union of the linked line segments $\mathcal{N}^{1D} = \bigcup_k T_k$. Let $T_k = p_k + sw_k$, $s \in [0, l_k]$, be the natural parameterization of the line segment $T_k$, $p_k$ being one endpoint of the segment. We define the 1D magnetization on the segment $T_k$ as the average value of the magnetization over $O_k$:

$$M^{1D}_k(s, t) := \frac{1}{|O_k|} \int_{(p_k + sw_k) \times O_k} M(r, t) \, dr.$$
It is easy to show that $M^{1D}_k(s,t)$ satisfies the 1D Bloch-Torrey PDE:

$$\frac{\partial}{\partial t} M^{1D}_k(s,t) = -I \gamma f(t) G(p_k + sw_k) M^{1D}_k(s,t) + D^0 \frac{\partial^2}{\partial s^2} M^{1D}_k(s,t).$$  \hspace{1cm} (4)

Two conditions have to be imposed on any intersection point $r$ of several line segments, $r = \cap_{k \in K} T_k$. The first condition is the continuity of the magnetization:

$$M^{1D}_k(r,t) = M^{1D}_{k'}(r,t), \quad k, k' \in K. \hspace{1cm} (5)$$

The second condition is the Kirchhoff law ensuring the conservation of flux:

$$\sum_{k \in K} D^0 \frac{\partial}{\partial s'} M^{1D}_k(r,t) = 0, \hspace{1cm} (6)$$

where $s' = s$ if $r = p_k$ is the starting point of the segment, $s' = -s$ otherwise.

Then we formulate the interface conditions linking the soma to the neurites. Suppose $I$ is the intersection between the soma $S$ and the neurite segment $B_k$ (there may be several such segments that extend out from the soma). Without loss of generality, we assume the parameterization variable $s = 0$ at the intersection is the starting point of the line segment $T_k$, then it can be shown that the following conditions hold:

$$\frac{1}{|I|} \int_I M_S(r,t) dr = M^{1D}_k(0,t), \hspace{1cm} (7)$$

and

$$\frac{1}{|I|} \int_I D^0 \nabla M_S(r,t) \cdot w_k = D^0 \frac{\partial}{\partial s} M^{1D}_k(0,t), \hspace{1cm} (8)$$

where $w_k$, parallel to $T_k$, is also the normal vector pointing outward from the soma at $I$. From Eqs. (3, 7), we can deduce that the initial condition on the 1D neurites should be $M^{1D}_k(s,0) = 1$. We call the model described above the 3D+1D model.

In the 3D+1D model, the dMRI signal is obtained from the 3D solution in the soma, $M_S$, and the 1D solution in the neurites, $M^{1D}_k, \quad k = 1, 2, \ldots$

$$S^{3D+1D}(b) := \frac{1}{|S| + \pi r^2} \sum_{k} \left( \int_S M_S(r,TE) dr + \pi r^2 \sum_k \int_0^{l_k} M^{1D}_k(s,TE) ds \right).$$

We emphasize that the solutions in the soma and in each of the line segments are linked to each other via the interface conditions of the PDE formulation.

4. Numerical results

The dMRI signal of the 3D+1D model was obtained and compared to that of the full 3D model. Both were computed using the code described in [7] on a Dell Precision M4700 laptop (Intel(R) Core(TM) i7-3740QM CPU @ 2.70GHz). We set the PGSE sequence to have a fixed pulse duration $\delta = 2.5$ms and varied $\Delta$. The dMRI signal at
8 $b$-values, $b = 0, 100, 500, 1000, 1500, 2000, 2500, 3000 \text{s/mm}^2$, was computed. The same intrinsic diffusion coefficient $D^0 = 3 \cdot 10^{-3} \text{mm}^2/\text{s}$ was used for all the simulations. We constructed a sample neuron geometry (shown in Fig. 2a) consisting of a spherical soma and two dendrite trees. We set the soma radius to $R = 10 \mu\text{m}$ and the neurite radius to $r = 1 \mu\text{m}$ [2]. The length of the dendrite segments varies from $50 \mu\text{m}$ to $112.5 \mu\text{m}$ and the total length of the two dendrite trees is $2272 \mu\text{m}$. This neuron comprises of 63% neurites and 37% soma by volume.

The 3D simulation in the full neuron took about 30 minutes on a finite elements mesh with 11314 vertices, where the mesh in the soma contains 1666 vertices. The simulation of the 3D+1D model (while keeping the same 3D mesh in the soma) took about 5 minutes.

We show the dMRI signals of the full 3D model and the 3D+1D model in Fig. 3a for $\Delta = 2.5 \text{ms}$ and in Fig. 3b for $\Delta = 100 \text{ms}$, in the gradient direction $\mathbf{g}/|\mathbf{g}| = (1, 1, 1)/\sqrt{3}$. We computed the relative difference in the $L^2$ norm between the signals to be 7% at the shorter diffusion time ($\Delta = 2.5 \text{ms}$) and 1% at the longer diffusion time ($\Delta = 100 \text{ms}$). As expected, the 1D approximation on the neurites works better when the transverse diffusion is negligible. For a given neurite radius, the longer the diffusion time, the better the approximation of the full 3D model by the 3D+1D model (compare Fig. 3a and Fig. 3b). For a given diffusion time, the approximation is better at lower gradient strengths: at $\Delta = 100 \text{ms}$, the two signals look indistinguishable in Fig. 3c, where only $b \in [0, 3000] \text{s/mm}^2$ is shown. However, at very high $b$-values, $b \in [0, 20000] \text{s/mm}^2$, shown in Fig. 3c, some differences in the signals become visible. When the neurite radius is larger, the transverse diffusion is more significant than when the neurite radius is smaller. So when the neurite radius is increased to $r = 2 \mu\text{m}$, the difference in the signals is larger than when $r = 1 \mu\text{m}$ (see Fig. 3d). The difference between the dMRI signals of the full 3D model and the 3D+1D model is 28% at $\Delta = 2.5 \text{ms}$ and 3% at $\Delta = 100 \text{ms}$ (compare to 7% and 1% for $r = 1 \mu\text{m}$). It is worth noting that the transverse diffusion in cylinders can be analytically included into the dMRI signal because many analytical results exist for the dMRI signal inside impermeable disks (see [5] and references therein).

5. Conclusion

We proposed a 3D+1D model to compute the dMRI signal arising from a single neuron by replacing the 3D simulation in the full neuron by a 3D simulation in the soma and 1D simulations in the neurites and linking them by the appropriate interface conditions. We showed that the 3D+1D model is computationally much faster to simulate than the full 3D model and still gives accurate results under a wide range of parameters. The 3D+1D model is accurate when the contribution to the dMRI signal from transverse diffusion in the neurites is negligible, i.e., at longer diffusion times, smaller neurite radii, and lower gradient strengths. In addition to computational advantages, the 3D+1D model, being more amenable to theoretical analysis due to the existence of (semi-)analytical results about diffusion in line segments, disks, and spheres, may be potentially exploited to produce semi-analytical expressions for the dMRI signal in neurons.
Figure 3: The dMRI signals inside the neuron shown on Fig. 2a in the gradient direction $g/|g| = (1, 1, 1)/\sqrt{3}$ at two diffusion times: $\Delta = 2.5\text{ms}$ (3a) and $\Delta = 100\text{ms}$ (3b) for neurites with radius $r = 1\mu\text{m}$, at very high $b$-values (3c), and for neurites with radius $r = 2\mu\text{m}$ (3d).

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