Microstructure Information from Diffusion Imaging

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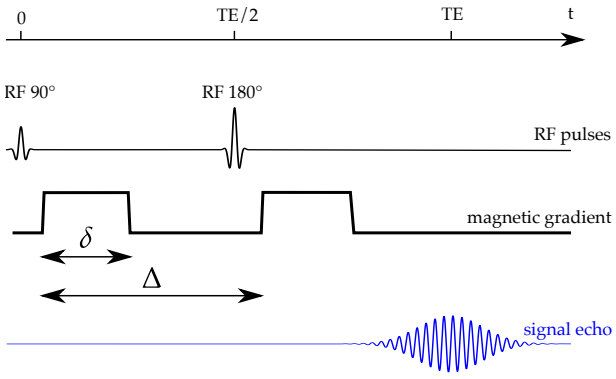
Abstract

Diffusion magnetic resonance imaging is an *in-vivo* and non-invasive imaging modality that can be used to probe the microstructure of biological tissues. Magnetization is made sensitive to the diffusion of water molecules in the brain. Water trapped in tissues with impermeable membranes is subject to restricted diffusion, which depends on the geometry of the tissue. Brain white matter is essentially composed of axons and glial cells which form the connections between neurons. Axons can be modeled as cylindrically-shaped tissue compartments while glial cells can be modeled as spherically-shaped tissue compartments. A number of models have been devised in the literature to predict the magnetization decay induced by such compartments. These models are either based on the approximations of the solution of the Bloch-Torrey equation, which describes the evolution of the magnetization in the presence of diffusion or on the Gaussian phase approximation of the magnetization decay or on the restricted diffusion between two parallel planes. These models are often fitted to the diffusion signal to provide so-called microstructural parameters such as the axon diameter or the axon density. Yet, there is currently no user-friendly way of understanding whether the acquired data is sensitive enough to the microstructural parameters of interest. The present work is an attempt to fill in this gap, by providing the Shiny application **midi** and its companion eponymous R package that allow to simulate the MR signal for a given set of microstructural parameters. The application features theoretical summaries of the existing models along with key visualizations of the signal they predict to help understanding the sensitivity of the MR signal to a parameter of interest, for a given set of experimental conditions.
Keywords : brain imaging - diffusion MRI - biophysical tissue models - Shiny - R6.

Theory

Diffusion MRI

Images of diffusion MRI are often acquired using the pulse-gradient spin-echo (PGSE) sequence. The sequence is based on the application of two diffusion-sensitizing gradient pulses in direction $\mathbf{n}$ with intensity G during a pulse duration δ and separated by a diffusion time Δ. The following figure illustrates the sequence:



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Models of restricted diffusion

We focus here on the signal attenuation induced by diffusion in the presence of tissue compartments with cylindrical geometry which is a fair approximation of the axon geometry. Let $\mathbf{u} \in \mathbb{S}^2$ and $R > 0$ be the axis and the radius of the cylinder, respectively. Let also D_0 be the coefficient associated with free diffusion in the cylinder. The signal attenuation $S(\delta, \Delta, G)$ induced by diffusion in the presence of tissue compartments with cylindrical geometry is assumed to be the product of the signal attenuation $S_{\parallel}(\delta, \Delta, G)$ induced by diffusion parallel to the cylinder axis and the signal attenuation $S_{\perp}(\delta, \Delta, G)$ induced by diffusion perpendicular to the cylinder axis (Assaf et al. 2004).

Diffusion parallel to the cylinder axis is assumed to be free and therefore usually modeled as a 1-dimensional Gaussian process inducing a mono-exponential signal decay, which reads:

$$S_{\parallel}(\delta, \Delta, G, \mathbf{n}; \mathbf{u}, D_0) = e^{-b(\delta,\Delta,G) D_0 \langle \mathbf{n}, \mathbf{u} \rangle^2},$$

where $b(\delta, \Delta, G) = \gamma^2 \delta^2 G^2 (\Delta - \delta/3)$ is the b-value, with γ the gyromagnetic ratio of the proton.

Diffusion perpendicular to the cylinder axis is assumed to be restricted and a number of models have been proposed to describe the signal attenuation induced by this type of diffusion. They are either based on approximations of the solution of the Bloch- Torrey equation under the narrow-pulse approximation (NPA), which assumes that no-diffusion occurs during the pulse duration δ (Söderman and Jönsson 1995; Callaghan 1995), or on the Gaussian phase approximation (GPA) of the magnetization decay (Neuman 1974; Vangelderen et al. 1994) or on a geometry simplification pertaining to studying restricted diffusion between two parallel planes (Stanisz et al. 1997).

A common feature of these models is that they predict the signal attenuation to be a function of the experimental parameters δ, Δ and G and the tissue properties such as the axon axis $\mathbf{u}$, the axon radius R, the axon density or the free diffusion coefficient D_0. However, there is currently no user-friendly way of understanding whether the acquired data is sensitive enough to the tissue properties of interest. The following sections describe the structure of the Shiny application **midi** and its companion eponymous R package that allow to simulate the MR signal for a given set of tissue properties and experimental conditions.

The midi application

Theory

A first tab of the application provides a tabset of focused one-page summaries on

1. *Diffusion imaging* to introduce the user to the basics of diffusion MRI and the notation of the experimental parameters;
2. *Models of restricted diffusion* to introduce the user to the existing models of restricted diffusion and the notation of the tissue properties;
3. *CHARMED* to introduce the user to the CHARMED model and optimized acquisition schemes for estimating the axon diameter and the axon density (Assaf et al. 2004);
4. *References values* to provide the user with reference or range values of the tissue properties and experimental parameters.

Axon diameter

A second tab of the application allows the user, through an embedded Shiny application, to simulate the MR signal for a given set of tissue properties and experimental conditions and to visualize the signal decay as a function of axon diameter. This is meant to understand the sensitivity of the MR signal to the axon diameter. In particular, if the signal decay remains approximately constant in the range of biologically plausible axon diameters, then one can conclude that the MR signal produced by a given set of experimental conditions and other tissue properties is not sensitive to the axon diameter.

Specifically, the user can control the experimental parameters δ, Δ and G and the angle between the axon axis $\mathbf{u}$ and the direction $\mathbf{n}$ of the applied diffusion-sensitizing gradient but the other tissue properties are set to biologically plausible values internally.

Axon density

A third tab of the application allows the user, through an embedded Shiny application, to simulate the MR signal for a given set of tissue properties and experimental conditions and to visualize the signal decay as a function of axon density. This is meant to understand the sensitivity of the MR signal to the axon density. In particular, if the signal decay remains approximately constant in the range of biologically plausible axon densities, then one can conclude that the MR signal produced by a given set of experimental conditions and other tissue properties is not sensitive to the axon density.

Specifically, the user can control the experimental parameters δ, Δ and G, the angle between the axon axis $\mathbf{u}$ and the direction $\mathbf{n}$ of the applied diffusion-sensitizing gradient, the axon diameter and the free diffusion coefficient D_0. The user can also apply a tortuosity model to account for the effect of the extra-axonal space on the MR signal.

The midi R package

The package provides the user with a set of functions to simulate the MR signal. The package relies on the R6 class system from the R package **R6** to define classes for each model of restricted diffusion. The package also relies on the R package **ggplot2** to visualize the MR signal decay. The package is available on GitHub and can be installed using the R package **devtools** as follows:

```
# install.packages("devtools")
devtools::install_github("astamm/midi")
```

Classes are designed to separate the tissue model parameters from the experimental parameters. In particular, each class has a constructor that takes as arguments the geometrical properties of the tissue in which diffusion is being modeled. There is then a single method `get_signal()` which takes as arguments the experimental parameters δ, Δ and G and returns the MR signal.

References

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