PhD project

Non-perturbative study of the Bloch-Torrey equation associated to the diffusion magnetic resonance imaging

under supervision by Denis GREBENKOV

Laboratory of Condensed Matter Physics, Ecole Polytechnique, Palaiseau, France

Summary:

Diffusion Magnetic Resonance Imaging (dMRI) is an imaging modality with numerous applications in medicine, biology and material sciences[1,2,3]. When molecules diffuse inside a heterogeneous medium (such as a biological tissue or a porous medium, see Fig. 1), the statistics of their random trajectories is affected by the presence of obstacles or interfaces. While these microscopic obstacles are not visible due to a limited spatial resolution of dMRI, their geometrical features are statistically aggregated into the macroscopic signal measured in dMRI. In other words, the signal provides an averaged information about a macroscopic volume (called a voxel) whose size is much larger than the characteristic scale of the microstructure. For instance, the size of cells in the brain varies from sub-microns (diameter of neurites) to tens of microns (diameter of neuronal bodies, axons and glial cells), while the typical voxel size is of the order of one millimeter. Measuring the macroscopic signal at various diffusion times and magnetic field gradients, one aims at revealing the morphological structure of the sample. This is a formidable inverse problem which, up to present, has no complete solution.

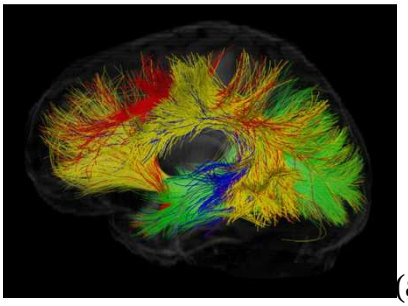
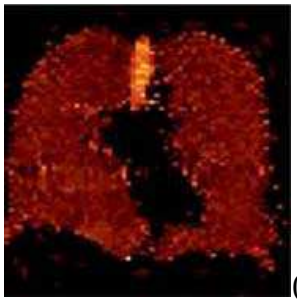
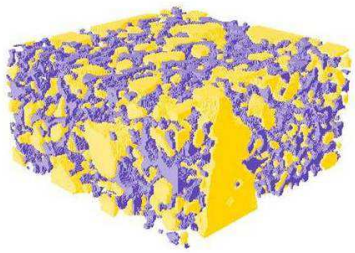

(a)

(b)

(c)

Figure 1: (a) Neuronal fibers detected by dMRI *in vivo*; (b) Map of apparent diffusion coefficients in the healthy human lungs obtained by dMRI *in vivo*; (c) Three-dimensional reconstruction of the microstructure of a cement paste obtained by a micro-CT imaging. Water molecules diffuse inside pores (in violet) formed in the solid phase (in yellow). This image illustrates the complicated organization of a porous medium whose microscopic structure is not directly accessible by dMRI. In turn, one aims at inferring the geometrical properties of this structure by monitoring diffusion of water molecules inside it.

When the microstructure of the medium is known, the macroscopic signal can be found by solving the Bloch-Torrey equation[2]

$$\frac{\partial M(\boldsymbol{r},t)}{\partial t} = -i\,\gamma(\boldsymbol{g}\cdot\boldsymbol{r})f(t)M(\boldsymbol{r},t) + D\nabla^2 M(\boldsymbol{r},t) \qquad (1)$$

which describes the evolution of the complex-valued transverse magnetization $M(\boldsymbol{r},t)$ due to encoding by inhomogeneous magnetic field (first term) and diffusion (second term). Here i is the imaginary unit, γ is the gyromagnetic ratio, D is the diffusion coefficient, $\boldsymbol{g}$ is the gradient of the applied magnetic field, and $f(t)$ is its temporal profile. The initial magnetization is uniform. The microstructure of the medium is represented by the interfaces (cellular membranes) or frontiers (solid-liquid) which hinder diffusion of the nuclei, and is incorporated through the boundary conditions

$$D\partial_n M_+(\boldsymbol{r},t) = -D\partial_n M_-(\boldsymbol{r},t) = \kappa(M_-(\boldsymbol{r},t) - M_+(\boldsymbol{r},t)), \qquad (2)$$

where ∂_n is the normal derivative, κ is the interface permeability, and $M_\pm(\boldsymbol{r},t)$ is the magnetization at two sides of the interface. The macroscopic signal S is then obtained by integrating $M(\boldsymbol{r},t)$ over the voxel. The dynamical and physiological parameters (D and κ), as well as the microstructure, enter into the macroscopic signal *implicitly*. Inferring these characteristics from the signal S, measured at variable diffusion times and/or applied magnetic fields (gradient $\boldsymbol{g}$ and/or its profile $f(t)$), presents a major challenge.

Numerous theoretical, numerical and experimental works have been undertaken to solve this fundamental problem[1,2,3]. The principal progress is achieved by the perturbative analysis at weak gradients (small $\boldsymbol{g}$). However, the validity of the perturbative analysis is limited, so that the behavior of the signal at high gradients, as well as the relation to the microstructure, remain poorly understood. At the same time, experiments suggest that higher gradients allow one to reveal finer geometrical details of the microstructure. While modern dMRI scanners can generate high enough gradients, the actual theory does not help much to interpret these measurements. The goal of the PhD thesis consists in developing a non-perturbative approach to study the macroscopic signal in porous media at high gradients and to reveal the role of the microstructure.

The PhD project will include the following steps (i) to generalize one-dimensional non-perturbative solutions[4,5] to higher dimensions (notably, to dimensions two and three which are relevant for applications); (ii) to combine the non-perturbative technique with statistical methods in order to describe the signal in disordered porous media; (iii) to propose approximate formulas for the signal at high gradients; (iv) to identify the principal geometrical characteristics of the medium that affect the signal in this regime; and (v) to validate these results by numerical simulations[6] in model media (such sphere packs, Voronoi cells, fractal forms, etc., see Fig. 2).

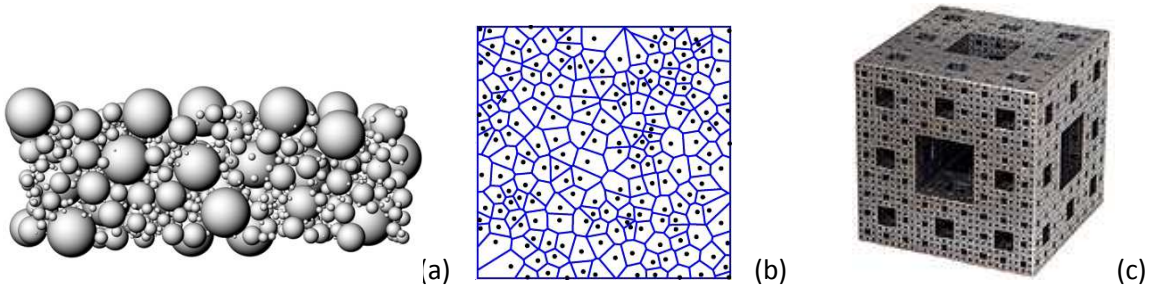


Figure 2: Examples of model porous media suitable for numerical simulations: sphere packs (a), Voronoi cells (b), Menger sponge (c).

References:

[1] P. T. Callaghan, *Principles of Nuclear Magnetic Resonance Microscopy* (Clarendon Press, Oxford, 1991).
[2] D. S. Grebenkov, *NMR survey of reflected Brownian motion*, Rev. Mod. Phys. **79**, 1077-1137 (2007).
[3] D. Le Bihan, H. Johansen-Berg, *Diffusion MRI at 25: Exploring brain tissue structure and function*, NeuroImage **61**, 324-341 (2012).
[4] S. D. Stoller, W. Happer, F. J. Dyson, *Transverse spin relaxation in inhomogeneous magnetic fields*, Phys. Rev. A **44**, 7459 (1991).
[5] D. S. Grebenkov, *Exploring diffusion across permeable barriers at high gradients. II. Localization regime*, J. Magn. Reson. **248**, 164-176 (2014).
[6] D. V. Nguyen, J.-R. Li, D. S. Grebenkov, and D. Le Bihan, *A finite elements method to solve the Bloch-Torrey equation applied to diffusion magnetic resonance imaging*, J. Comput. Phys. **263**, 283-302 (2014).