Journal of Magnetic Resonance 220 (2012) 85–93

Contents lists available at SciVerse ScienceDirect

Journal of Magnetic Resonance

journal homepage: www.elsevier.com/locate/jmr

Anisotropy in high-resolution diffusion-weighted MRI and anomalous diffusion

A. Hanyga [a,*], M. Seredyńska [b,*]

[a] ul. M.Grzegorzewskiej 6 m. 70, 02-778 Warszawa, Poland
[b] ul. Bitwy Warszawskiej 1920 r. 14 m. 52, 02-366 Warszawa, Poland

ARTICLE INFO

Article history:
Received 8 March 2012
Revised 30 April 2012
Available online 14 May 2012

Keywords:
Diffusion-weighted MRI
Anisotropy
Non-locality
Fractional derivative
Anomalous diffusion
Stejskal–Tanner formula

ABSTRACT

It is shown below that complex diffusion anisotropy observed in diffusion-weighted MRI can be fully accounted for by allowing for non-locality of the spatial operator in the diffusion equation. The anisotropy is represented by a distribution over directions on a sphere. It allows recognition of fiber tracts crossing at arbitrary angles. A simple generalization of the Stejskal–Tanner equation for the determination of the ODF is presented. Furthermore, an explicit solution of the Bloch–Torrey equation for an anisotropic time-fractional diffusion equation is obtained in terms of a generalized Mittag–Leffler type function.

1. Introduction

The Apparent Diffusion Coefficient (ADC) of water in a structurally complex environment of a cell or tissue is strongly anisotropic due to the restrictions of water motion imposed by cell membranes, ligaments, etc. In MRI the ADC is estimated by comparing the reaction of magnetization to two successive magnetic field pulses that would cancel each other in the absence of diffusion. The magnetic pulses are inhomogeneous in the space. For simplicity they have a constant gradient that varies in time. Due to its displacement in the inhomogeneous magnetic field the hydrogen atom is subjected to two successive magnetic pulses that do not cancel each other. The mismatch depends on the range of diffusion and on the direction of the magnetic field gradient relative to the direction of diffusive motion. The direction of the magnetic field gradient **g** is used to probe various directions of diffusion in the tissue.

In Diffusion Tensor Imaging (DTI) the anisotropy of the diffusive flux is assumed to be represented by a rank-2 diffusion tensor. The signal attenuation in the Stejskal–Tanner formula is given by an exponential of the associated quadratic form in the components of the field gradient vector.

The observed anisotropy pattern of diffusion is however quite complex and cannot be described by quadratic polynomial. In applications to tractographic reconstruction of fiber tracts this model provides only one direction of enhanced diffusivity – the direction of the eigenvector corresponding to the largest eigenvalue. As a result it is possible to identify at most one fiber tract direction in each voxel and fiber crossings cannot be detected.

The results of high-resolution MRI scanning of brain and bio-tissues indicate the need for higher-order anisotropy of diffusion coefficients in the Stejskal–Tanner formula [1]. In order to account for observed anisotropy Özarslan and Mareci expressed the signal attenuation in the Stejskal–Tanner formula in terms of polynomials of arbitrarily high degree in the magnetic field gradient.

Alternative methods have been suggested to detect higher-order anisotropy such as q-space imaging [2,3] or Q-ball imaging [4] and their modifications. Our method is based on a modification of the Stejskal–Tanner formula and will therefore be compared with [1].

The Stejskal–Tanner formula can be derived from the Bloch–Torrey equation describing diffusion of protons in a constant gradient magnetic field. The observed dependence of the MR signal on the direction of the field gradient must be accommodated in the anisotropy of the diffusion equation. Özarslan and Mareci suggested an ad hoc diffusion equation with diffusion coefficient dependent on the direction of the magnetic gradient. This model is however inconsistent with Torrey's extension of the Bloch equations [5]. It is shown here that the same anisotropy pattern can be explained by an anisotropic superdiffusion model. In contrast to [1] in our model the b factor involves the gradient amplitude g_0 raised to the power α, with a new diffusion parameter $\alpha \leqslant 2$, while in their paper b involves the square of g_0. Apart from that the conclusions for tractographic reconstruction of fiber bundles or for mapping scalar anisotropy measures (see [1,6,7]) are the same in both papers.

* Corresponding authors. Address: ul. M. Grzegorzewskiej 6 m. 70, 02-778 Warszawa, Poland
E-mail addresses: ajhbergen@yahoo.com (A. Hanyga), msered@ippt.gov.pl (M. Seredyńska).

1090-7807/$ - see front matter © 2012 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.jmr.2012.05.001

Notation

$\mathbb{R}^d$	the space of d-tuples of reals $\{x_1,\dots,x_d\}$
$\mathrm{d}_d x$	$\mathrm{d}x_1\dots\mathrm{d}x_d$
$\int\dots\mathrm{d}_d x$	$\int_{\mathbb{R}^d}\dots\mathrm{d}_d x$
$\mathbf{v}\cdot\mathbf{w}:=\sum_{i=1}^d v_i w_i$	scalar product of two vectors
I^α	fractional integral operator (defined in the paper)
D^α	fractional differential operator (defined in the paper)

$\tilde f(p):=\int_0^\infty \mathrm{e}^{-pt}f(t)\mathrm{d}t$ Laplace transform
$f*_t g(t):=\int_0^t f(s)g(t-s)\mathrm{d}s$;
$\hat f(\mathbf{k}):=\int \mathrm{e}^{\mathrm{i}\mathbf{k}\cdot x}f(x)\mathrm{d}_d x$ Fourier transform
$f*_x g(x):=\int f(x')g(x-x')\mathrm{d}_d x'$ (integration over the entire space)

In this paper water diffusion in tissue is represented by a pseudo-differential operator of order $\alpha\leqslant 2$ which has the required anisotropic properties. The proposed operator is non-local. In the absence of anisotropy it reduces to a fractional power of the Laplacian $-\mathcal{D}(-\nabla^2)^\gamma$, where $0<\gamma\leqslant 1$ and $\mathcal{D}$ is a positive constant. Our proposal is thus an extension of the anomalous diffusion model introduced in order to explain observed deviations from the classical Stejskal–Tanner formula [8–10]. For $\alpha=2$ it reduces to diffusion with tensorial anisotropy. For $\alpha<2$ the anisotropy is represented by a distribution of directions of diffusive motion expressed by a measure on the unit sphere.

The pseudo-differential operators discussed in this paper are parameterized by a measure m on the unit sphere. This measure replaces the more crude tensorial representation of the dependence of the MR signal on the direction of the field gradient in DTI. The Stejskal–Tanner formula can be used to sample the measure m. By an analysis of the flux density operator it is argued that the maxima of the density H of m represent the directions of maximum diffusivity and thus can be associated with the directions of fiber tracts or channels.

The maxima of the density H can be searched by a peak searching algorithm. We therefore discuss some issues involving interpolation of H.

The solution of the same problem for a time-fractional diffusion equation is also presented. The solution is expressed in terms of a Mittag–Leffler type function instead of the exponential. The Stejskal–Tanner formula for this case is therefore much more complicated and is not presented in this paper.

2. The anomalous diffusion equation

It has already been noticed earlier that the observed attenuation of the magnetization deviates from the classical Stejskal–Tanner formula. In order to account for this deviation Magin et al. [9] considered time-fractional diffusion equations $\mathrm{D}^\beta u=\mathcal{D}\nabla^2 u$ with $0<\beta\leqslant 1$, where D^β denotes the Caputo derivative [11,12], defined by the equation

$$\mathrm{D}^\beta u:=\mathrm{I}^{1-\beta}\mathrm{D}u,\quad 0<\beta\leqslant 1 \tag{1}$$

where the operator $\mathrm{I}^\gamma,\gamma>0$, defined by the formula

$$\mathrm{I}^\gamma u:=\int_0^t \frac{s^{\gamma-1}}{\Gamma(\gamma)}u(t-s)\mathrm{d}s \tag{2}$$

is the fractional integral operator. The positive constant $\mathcal{D}$ is a diffusion coefficient of dimension $[\mathrm{length}^2/\mathrm{time}^\beta]$.

A different generalization of the diffusion equation involves a pseudo-differential operator Q instead of $\mathcal{D}\nabla^2$:

$$\mathrm{D}\rho=Q\rho \tag{3}$$

with an initial condition $\rho(0,\mathbf{x})=\rho_0(\mathbf{x})$. The operator Q is a pseudo-differential operator such that Eq. (3) preserves positivity, i.e. every solution of Eq. (3) with non-negative initial data is non-negative.

A sufficiently large class of pseudo-differential operators Q of the required kind is defined by their symbol

$$\widehat{Q}(\mathbf{k})=-\int_{\mathcal{S}}|\mathbf{k}\cdot\mathbf{y}|^\alpha m(\mathrm{d}\mathbf{y}) \tag{4}$$

where $\mathcal{S}$ denotes the surface of the unit sphere centered at 0, m is a measure on the sphere and α is a parameter satisfying the inequalities $0<\alpha\leqslant 2$. The action of Q is defined by the equation

$$\int \mathrm{e}^{-\mathrm{i}\mathbf{k}\cdot\mathbf{x}}[Qf](\mathbf{x})\mathrm{d}x=\widehat{Q}(\mathbf{k})\hat f(\mathbf{k}) \tag{5}$$

For $\alpha=2$

$$\widehat{Q}(\mathbf{k})=-\mathbf{k}^{\mathrm{T}}\mathbf{A}\mathbf{k}$$

and

$$Q=-\nabla^{\mathrm{T}}\mathbf{A}\nabla \tag{6}$$

where

$$\mathbf{A}:=\int_{\mathcal{S}}\mathbf{y}\mathbf{y}^{\mathrm{T}}\mu(\mathrm{d}\mathbf{y}) \tag{7}$$

is a positive semi-definite matrix. In this case we are back in the framework of DTI.

The operators defined by (4) are a special class of generators of α-stable Lévy processes. All the operators in this class are positivity preserving [13]. An independent proof of this property, based on the theory of non-local diffusion equations, is given Appendix A.

A further generalization of Eq. (3)

$$\mathrm{D}^\beta\rho=Q\rho,\ 0<\beta\leqslant 1 \tag{8}$$

with an initial condition $\rho(0,\mathbf{x})=\rho_0(\mathbf{x})$ will also be discussed. It follows from an integral representation of solutions of Eq. (8) in [14] that the solutions of Eq. (8) with non-negative initial data are non-negative if Eq. (3) has this property (see B).

A special case of (8) is the time–space fractional diffusion equation

$$\mathrm{D}^\beta\rho=-\mathcal{D}\,(-\nabla^2)^{\alpha/2}\rho \tag{9}$$

with $\mathcal{D}>0$ of dimension $[\mathrm{length}^\alpha/\mathrm{time}^\beta], 0<\beta\leqslant 1, 0<\alpha\leqslant 2$ [14]. The expression on the right-hand side is defined by its Fourier transform $|\mathbf{k}|^\alpha\hat\rho(t,\mathbf{k})$. In one-dimensional space eq. (9) reduces to the equation

$$\mathrm{D}^\beta\rho=\mathcal{D}\,{}^{\mathrm{R}}\mathrm{D}^\alpha\rho \tag{10}$$

considered in [9], where ${}^{\mathrm{R}}\mathrm{D}^\alpha f$ denotes the Riesz derivative of $f(x)$ defined by its Fourier transform $|k|^\alpha\hat f(k)$ [11,15].

Eq. (10) can be derived from CTRWs (Continuous Time Random Walks, [16]), in which the time-fractional aspect is linked to long waiting times for a trapped particle to escape, while the space-fractional aspect is associated with availability of long jumps whose lengths are distributed according to a probability density that does not have a finite variance. The traps slow the diffusion giving rise to subdiffusion, for which there is ample evidence in bio-tissue [17]. Availability of long jumps alone (Lévy flights) results in superdiffusion. Combining the two mechanisms may give rise to either of these regimes. Another background for Eq. (10) involves fractal structure and self-similarity [18]. For the solutions of Eq. (9) or