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Research paper

Exact solutions to the fractional time-space Bloch–Torrey equation for magnetic resonance imaging

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ABSTRACT

The quantification of anomalous diffusion is increasingly being recognised as an advanced modality of analysis for the evaluation of tissue microstructure in magnetic resonance imaging (MRI). One powerful framework to account for anomalous diffusion in biological and structurally heterogeneous tissues is the use of diffusion operators based on fractional calculus theory, which generalises the physical principles of standard diffusion in homogeneous media. However, their non-locality makes analytical solutions often unavailable, limiting the applicability of these modelling and analysis techniques. In this paper, we derive compact analytical signal decays for practical MRI sequences in the anisotropic fractional Bloch–Torrey setting, as described by the space fractional Laplacian and importantly the time Caputo derivative. The attained solutions convey relevant characteristics of MRI in biological tissues not replicated by standard diffusion, including super-diffusive and sub-diffusive regimes in signal decay and the diffusion-driven incomplete refocusing of spins at the end of the sequence. These results may therefore have significant implications for advancing the current interpretation of MRI, and for the estimation of tissue properties based on exact solutions to underlying diffusive processes.

1. Introduction

Nowadays, water-diffusion magnetic resonance imaging (MRI) has been consolidated as an unparalleled technology for the evaluation of pathological disarrangements in tissue microstructure in different organs and diseased conditions. In spite of their promising results in clinical applications, a limitation of conventional MRI diffusion metrics is that they are derived based on the assumptions of Gaussian diffusion. However, biological tissues are known to be structurally complex environments, where many factors affect the decay of the diffusion signal. These include the dissimilar sizes of the intracellular and extracellular compartments involved in water exchange, the existence of different tissue types, highly inhomogeneous extracellular matrices and intricate microvasculature networks within the organs, or the presence of cellular membranes as well as fibre and laminar tissue structures that act as effective barriers hindering the diffusion of water molecules [1,2]. As a result, and in particular under large diffusion weighting gradients, the acquired diffusion signal deviates from the mono-exponential decay predicted by Gaussian diffusion in a phenomenon known as anomalous diffusion. Quantification of such an anomalous signal decay has shown higher sensitivity and to provide complementary information for detecting

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pathological conditions to that encapsulated by standard diffusion metrics. Whereas the majority of studies to date have been conducted in the field of neuroscience (see [3] and references therein for a comprehensive review on the brain and spine), applications also include the assessment of myocardial heterogeneity in the heart [4], liver fibrosis [5] and cartilage degradation [6], to cite a few.

In recent years, fractional calculus has arisen as a powerful and robust theoretical framework in order to account for the effects of anomalous diffusion in MRI [7–12]. The main advantage of such an approach is that insights can be derived from generalisations of the physical principles describing the magnetisation of water protons in MRI: the Bloch–Torrey equation [13]. This can have important implications in understanding the different contributions of tissue microstructure to anomalous diffusion [14], compared to the fitting of experimental data to phenomenological signal decays such as bi-exponential [15] or stretched-exponential models [16]. However, an important drawback of the fractional setting is the complexity of its associated non-local operators for the derivation of exact solutions for the acquired signal decay. Whereas the purely space fractional setting imposes no real difficulties when using Fourier transforms [10,17], the time fractional setting is much more complicated, and to derive an analytical solution to the full fractional time-space Bloch–Torrey equation still remains as an open challenge [10].

In this paper, we derive such an exact solution by exploiting the piecewise and polynomial nature of practical MRI pulse sequences. Here, we focus on the space fractional Laplacian and the time Caputo derivative given their suitability for the description of physical problems. The associated non-autonomous fractional differential equations are then solved using extended (Kilbas–Saigo) Mittag–Leffler and Lauricella functions. Through the connection of the latter with Gauss hypergeometric functions, we additionally derive compact analytical formulas for the acquired signal decay at the end of the pulse sequence. The attained solutions not only replicate the super-diffusive and sub-diffusive regimes reported in signal decay in biological tissues, but also the diffusion-driven residual phase shift linked to the incomplete refocusing of spins at the end of the encoding sequence. Our results may therefore have important implications for advancing the interpretation of MRI and the characterisation of tissue microstructure in healthy and diseased states, through the estimation of tissue properties based on exact solutions to the underlying diffusive processes.

2. Theory

In the traditional diffusion setting, the dynamics of the diffusion weighted signal S are described by the standard Bloch–Torrey equation [13]:

$$\partial_t S = -i\gamma \mathbf{r}\cdot\mathbf{G}(t)\,S + \nabla\cdot\mathbf{D}\nabla S, \tag{1}$$

where i is the imaginary unit, $\mathbf{r}$ is the position vector, γ is the gyromagnetic ratio for protons, $\mathbf{G}(t)$ is the time-varying applied gradient, and $\mathbf{D}$ is a positive definite symmetric diffusion tensor. Analytical solutions for the signal decay can be obtained by assuming solutions of the form

$$S(\mathbf{r},t) = S_0 A(t)\varphi(\mathbf{r},t), \quad \varphi(\mathbf{r},t) = \exp\left(-i\mathbf{r}\cdot\mathbf{L}(t)\right), \quad \mathbf{L}(t) = \gamma\int_0^t \mathbf{G}(s)ds, \tag{2}$$

with $A(0)=1$, where S_0 is the baseline signal intensity. Inserting this ansatz into (1) yields

$$\frac{A'(t)}{A(t)} = -w(t), \tag{3}$$

with $w(t) = \mathbf{L}^T\cdot\mathbf{D}\mathbf{L}$, and straightforward solution in the form

$$A(t) = \exp\left(-\int_0^t w(s)ds\right). \tag{4}$$

Assuming the Stejskal–Tanner sequence [18], which as shown in Fig. 1 consists of a pair of opposed rectangular pulses of duration δ, separation Δ, amplitude G, and unit direction $\mathbf{g}$, then $w(t)$ becomes

$$w(t) = \mathbf{g}^T\mathbf{D}\mathbf{g}\left[\gamma\int_0^t |\mathbf{G}(s)|ds\right]^2 = \mathbf{g}^T\mathbf{D}\mathbf{g}\times\begin{cases} 0 & , \quad 0<t\le t_0 \\ (\gamma G)^2(t-t_0)^2 & , \quad t_0<t\le t_0+\delta \\ (\gamma G\delta)^2 & , \quad t_0+\delta<t\le t_0+\Delta \\ (\gamma G)^2(t_0+\Delta+\delta-t)^2 & , \quad t_0+\Delta<t\le t_0+\Delta+\delta \\ 0 & , \quad t_0+\Delta+\delta<t \end{cases} \tag{5}$$

(note that $\times$ denotes scalar and not cross vector product throughout this contribution). Integrating (4) through the different time intervals, the amplitude of the acquired signal at the end of the pulse sequence is given by the exponential decay

$$S/S_0 = \exp\left(-b\,\mathbf{g}^T\mathbf{D}\mathbf{g}\right), \tag{6}$$

where $b = (\gamma G\delta)^2(\Delta-\delta/3)$ is the so-called b value.