

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

Alfonso Bueno-Orovio^{a,*}, Kevin Burrage^{a,b,c}

^a*Department of Computer Science, University of Oxford, Oxford OX1 3QD, United Kingdom*

^b*ARC Centre of Excellence for Mathematical and Statistical Frontiers (ACEMS), Brisbane QLD 4001, Australia*

^c*School of Mathematical Sciences, Queensland University of Technology, Brisbane QLD 4001, Australia*

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.

Keywords: Anomalous diffusion, fractional calculus, magnetic resonance imaging

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 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

*Corresponding author

Email addresses: `alfonso.bueno@cs.ox.ac.uk` (Alfonso Bueno-Orovio), `kevin.burrage@qut.edu.au` (Kevin Burrage)

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]:

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

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

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

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

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

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

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

Assuming the Stejskal–Tanner sequence [18], which as shown in Figure 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

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

(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

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

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

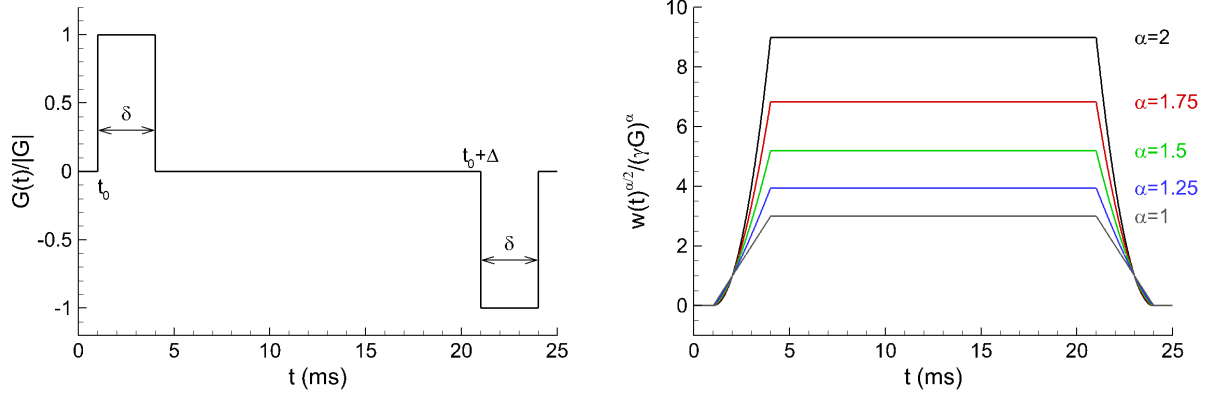


Figure 1: Normalised Stejskal–Tanner sequence (left panel) and normalised integrating function $w(t)^{\alpha/2}$ (right panel) for different values of the fractional power in space, α . Sequence parameters are $\delta = 3$ ms and $\Delta = 20$ ms.

3. Calculations

3.1. The fractional Laplacian case

In order to address the extension of the previous results to the full time-space fractional Bloch–Torrey setting, we first consider the space-fractional scenario, of a much easier analytical treatment than its time-fractional counterpart. In addition, this section will also introduce some of the elements required for the reformulation of the full time-space fractional case into a solvable version, circumventing the use of infinite series of fractional Riemann integral operators.

Among different approaches, the generalisation of the Bloch–Torrey equation to accommodate super-diffusive processes can be achieved by means of the space-fractional Laplacian

$$\partial_t S = -i\gamma \mathbf{r} \cdot \mathbf{G}(t) S - \tau_\alpha^{\alpha/2-1} (-\nabla \cdot \mathbf{D} \nabla)^{\alpha/2} S, \quad (7)$$

where $1 < \alpha \leq 2$ is the fractional power in space, and τ_α (units of time) is a positive scaling factor introduced to ensure the consistency of units. Unlike other fractional operators, the fractional Laplacian $(-\nabla \cdot \mathbf{D} \nabla)^{\alpha/2}$ has a straightforward connection with its non-fractional counterpart by means of its Fourier transform, defined as in the standard Laplacian but with eigenvalues raised to the fractional power $\alpha/2$ [17].

By the properties of the fractional Laplacian applied to the ansatz (2), one gets

$$(-\nabla \cdot \mathbf{D} \nabla)^{\alpha/2} S = -S_0 A(t) (-\nabla \cdot \mathbf{D} \nabla)^{\alpha/2} \varphi(\mathbf{r}, t) = -S_0 A(t) w(t)^{\alpha/2} \varphi(\mathbf{r}, t), \quad (8)$$

which reduces (7) to an equivalent expression for $A(t)$ to the standard diffusion case

$$\frac{A'(t)}{A(t)} = -\tau_\alpha^{\alpha/2-1} w(t)^{\alpha/2}, \quad (9)$$

with $w(t)^{\alpha/2}$ given for the Stejskal–Tanner sequence by

$$w(t)^{\alpha/2} = (\mathbf{g}^T \mathbf{D} \mathbf{g})^{\alpha/2} \times \begin{cases} 0 & , \quad 0 < t \leq t_0 \\ (\gamma G)^\alpha (t - t_0)^\alpha & , \quad t_0 < t \leq t_0 + \delta \\ (\gamma G \delta)^\alpha & , \quad t_0 + \delta < t \leq t_0 + \Delta \\ (\gamma G)^\alpha (t_0 + \Delta + \delta - t)^\alpha & , \quad t_0 + \Delta < t \leq t_0 + \Delta + \delta \\ 0 & , \quad t_0 + \Delta + \delta < t. \end{cases} \quad (10)$$

Integrating (9), the exact solution for the acquired signal in the fractional Laplacian setting is given by

$$S/S_0 = \exp \left(-\tau_\alpha^{\alpha/2-1} (\gamma G \delta)^\alpha \left(\Delta - \delta \frac{\alpha-1}{\alpha+1} \right) (\mathbf{g}^T \mathbf{D} \mathbf{g})^{\alpha/2} \right), \quad (11)$$

which for $\alpha = 2$ recovers the standard diffusion case, given by $S/S_0 = \exp(-b \mathbf{g}^T \mathbf{D} \mathbf{g})$, $b = (\gamma G \delta)^2 (\Delta - \delta/3)$.

3.2. The time-space fractional Bloch–Torrey equation

Analogous to the space fractional case, sub-diffusive processes can be accounted in the Bloch–Torrey equation by the use of time fractional operators

$$\tau_\beta^{\beta-1} \partial_t^\beta S = -i\gamma \mathbf{r} \cdot \mathbf{G}(t) S - \tau_\alpha^{\alpha/2-1} (-\nabla \cdot \mathbf{D} \nabla)^{\alpha/2} S. \quad (12)$$

Here, we focus on the fractional Caputo derivative of order $0 < \beta \leq 1$, defined as

$$\partial_t^\beta f(t) = \frac{1}{\Gamma(1-\beta)} \int_0^t \frac{1}{(t-s)^\beta} \frac{\partial f}{\partial s} ds, \quad (13)$$

where $\Gamma(z)$ is the Gamma function. As before, τ_β (units of time) represents a positive scaling factor introduced for consistency of units.

Lemma 1. For f, g differentiable functions, by the properties of the fractional Caputo derivative

$$\partial_t^\beta (af(t) + bg(t)) = a\partial_t^\beta f(t) + b\partial_t^\beta g(t), \quad (14a)$$

$$\partial_t^\beta t^q = \frac{\Gamma(1+q)}{\Gamma(1+q-\beta)} t^{q-\beta}, \quad \partial_t^\beta 1 = 0, \quad (14b)$$

$$\partial_t^\beta E_\beta(at^\beta) = aE_\beta(at^\beta), \quad (14c)$$

where $E_\beta(z) = \sum_{j=0}^{\infty} \frac{z^j}{\Gamma(1+j\beta)}$ is the one-parametric Mittag-Leffler function, $E_1(z) = \exp(z)$.

The non-local nature of the Caputo operator poses a number of challenges in the solution of this problem. For solutions of the form $S(\mathbf{r}, t) = S_0 A(t) \varphi(\mathbf{r}, t)$ as defined by (2), the definition of the fractional Laplacian given by (8) still holds, and therefore $-(\nabla \cdot \mathbf{D} \nabla)^{\alpha/2} S = -w(t)^{\alpha/2} S$. However, an immediate difficulty arises in the calculation of the Caputo derivative of the product of two functions, which is given by an infinite series of fractional Riemann integral operators [19, p. 59]. Instead of solving (12) in terms of $A(t)$, we decided to follow a different approach, performing the direct integration of $S(\mathbf{r}, t)$ through exploitation of the piecewise and polynomial nature of $\mathbf{G}(t)$ and $w(t)^{\alpha/2}$ in the Stejskal–Tanner sequence. By using the results presented in (10) from the previous section, this allows us to rewrite (12) as

$$\begin{aligned} \tau_\beta^{\beta-1} \partial_t^\beta S &= 0 & , \quad 0 < t \leq t_0 \\ \tau_\beta^{\beta-1} \partial_t^\beta S &= -i\gamma \mathbf{G} \mathbf{r} \cdot \mathbf{g} S - \tau_\alpha^{\alpha/2-1} (\mathbf{g}^T \mathbf{D} \mathbf{g})^{\alpha/2} (\gamma G)^\alpha (t - t_0)^\alpha S & , \quad t_0 < t \leq t_0 + \delta \\ \tau_\beta^{\beta-1} \partial_t^\beta S &= -\tau_\alpha^{\alpha/2-1} (\mathbf{g}^T \mathbf{D} \mathbf{g})^{\alpha/2} (\gamma G \delta)^\alpha S & , \quad t_0 + \delta < t \leq t_0 + \Delta \\ \tau_\beta^{\beta-1} \partial_t^\beta S &= i\gamma \mathbf{G} \mathbf{r} \cdot \mathbf{g} S - \tau_\alpha^{\alpha/2-1} (\mathbf{g}^T \mathbf{D} \mathbf{g})^{\alpha/2} (\gamma G)^\alpha (t_0 + \Delta + \delta - t)^\alpha S & , \quad t_0 + \Delta < t \leq t_0 + \Delta + \delta \\ \tau_\beta^{\beta-1} \partial_t^\beta S &= 0 & , \quad t_0 + \Delta + \delta < t. \end{aligned}$$

The second part of property (14b) implies that the signal remains constant when $\partial_t^\beta S = 0$, thus eliminating the need of considering the first and last time intervals. For each of the remainder intervals, the value of the solution at their end sets up the initial condition for the next part of the pulse sequence, with the final magnitude of signal decay given by the convolution of the magnitudes of all the consecutive individual solutions. Therefore, by treating the problems above as independent subproblems, each of them starting at $t = 0$ in order to further simplify the notation, equation (12) can be finally rewritten as the following three consecutive subproblems

$$\partial_t^\beta S_1 = (\mu + \lambda t^\alpha) S_1, \quad S_1(0) = S_0, \quad t \in (0, \delta], \quad (15a)$$

$$\partial_t^\beta S_2 = \lambda \delta^\alpha S_2, \quad S_2(0) = S_1(\delta), \quad t \in (0, \Delta - \delta], \quad (15b)$$

$$\partial_t^\beta S_3 = (-\mu + \lambda(\delta - t)^\alpha) S_3, \quad S_3(0) = S_2(\Delta - \delta), \quad t \in (0, \delta], \quad (15c)$$

where $\mu = -\tau_\beta^{1-\beta} i\gamma \mathbf{G} \mathbf{r} \cdot \mathbf{g}$, $\lambda = -\tau_\beta^{1-\beta} \tau_\alpha^{\alpha/2-1} (\mathbf{g}^T \mathbf{D} \mathbf{g})^{\alpha/2} (\gamma G)^\alpha$, with the total signal decay given by $S_3(\delta)$.

From the property (14c) of the fractional Caputo derivative, it is straightforward to see that the solution of problem (15b) in the central interval of the sequence is given by

$$S_2(t) = S_2(0)E_\beta(\lambda\delta^\alpha t^\beta), \quad (16)$$

which recovers the expected exponential decay in the case $\beta = 1$. To make headway in the solution of the fractional non-autonomous problems (15a) and (15c), we first address the following sequence of auxiliary problems.

Theorem 1 (Subproblem (15a), $\mu = 0$). *The solution of $\partial_t^\beta y = \lambda t^\alpha y$, $y(0) = y_0$, is*

$$y(t) = y_0 \sum_{j=0}^{\infty} \theta_j (\lambda t^{\alpha+\beta})^j \quad (17a)$$

with coefficients θ_j given by

$$\theta_j = \frac{\Gamma(1 + j(\alpha + \beta) - \beta)}{\Gamma(1 + j(\alpha + \beta))} \theta_{j-1} \quad (j \geq 1), \quad \theta_0 = 1. \quad (17b)$$

Proof This problem has been previously considered in the literature [20, pp. 232-233], although here we present an alternative proof for completeness and a closer connection with our later results. We assume solutions of the form

$$y(t) = y_0 \sum_{j=0}^{\infty} \tilde{\theta}_j t^{q_j},$$

where $\tilde{\theta}_0 = 1$, $q_0 = 0$ in order to satisfy the initial condition. Introduced in the problem equation, and by the properties of the Caputo derivative in Lemma 1, this yields

$$y_0 \sum_{j=1}^{\infty} \tilde{\theta}_j \frac{\Gamma(1 + q_j)}{\Gamma(1 + q_j - \beta)} t^{q_j - \beta} = y_0 \lambda \sum_{j=1}^{\infty} \tilde{\theta}_{j-1} t^{\alpha + q_{j-1}}.$$

Equating powers, we immediately see $q_j - \beta = \alpha + q_{j-1}$, and by recursion $q_j = j(\alpha + \beta)$. Furthermore,

$$\tilde{\theta}_j = \lambda \frac{\Gamma(1 + q_j - \beta)}{\Gamma(1 + q_j)} \tilde{\theta}_{j-1} = \lambda \frac{\Gamma(1 + j(\alpha + \beta) - \beta)}{\Gamma(1 + j(\alpha + \beta))} \tilde{\theta}_{j-1}.$$

The definition of the multiplicative factors $\rho_j = \frac{\Gamma(1 + j(\alpha + \beta) - \beta)}{\Gamma(1 + j(\alpha + \beta))}$, $\theta_j = \rho_j \theta_{j-1}$, completes the proof. \square

For $\beta = 1$, and recalling that $\Gamma(1 + z) = z\Gamma(z)$, coefficients $\theta_j = \frac{1}{j(1+\alpha)} \theta_{j-1} = \frac{1}{j!(1+\alpha)^j}$, and therefore

$$y(t) = y_0 \sum_{j=0}^{\infty} \frac{1}{j!} \left(\lambda \frac{t^{1+\alpha}}{1+\alpha} \right)^j = y_0 \exp \left(\lambda \frac{t^{1+\alpha}}{1+\alpha} \right),$$

which is the expected solution to $\partial_t y = \lambda t^\alpha y$, $y(t_0) = y_0$, in the standard diffusion in time case.

As an additional remark, solution (17a)–(17b) coincides with $E_{\beta, 1 + \frac{\alpha}{\beta}, \frac{\alpha}{\beta}}(\lambda t^{\alpha+\beta})$, where $E_{p,m,l}(z) = \sum_{j=0}^{\infty} c_j z^j$, $c_0 = 1$, $c_j = \prod_{k=0}^{j-1} \frac{\Gamma(1+p(km+l))}{\Gamma(1+p(km+l+1))}$ ($j \geq 1$), is the three-parametric (Kilbas–Saigo) generalised Mittag–Leffler function [21].

Theorem 2 (Subproblem (15a), $\mu \neq 0$). *The solution of $\partial_t^\beta y = (\mu + \lambda t^\alpha)y$, $y(0) = y_0$, is*

$$y(t) = y_0 \sum_{j=0}^{\infty} \sum_{k=0}^j \mu^{j-k} \lambda^k \theta_{j,k} t^{j\beta + k\alpha} \quad (18a)$$

with coefficients $\theta_{j,k}$ given by

$$\theta_{j,j} = \rho_{j,j} \theta_{j-1,j-1} \quad (j \geq 1), \quad \theta_{j,k} = \rho_{j,k} (\theta_{j-1,k-1} + \theta_{j-1,k}) \quad (1 \leq k < j), \quad \theta_{j,0} = \frac{1}{\Gamma(1 + j\beta)}, \quad (18b)$$

where the multiplicative factors $\rho_{j,k}$ are defined as

$$\rho_{j,k} = \frac{\Gamma(1 + (j-1)\beta + k\alpha)}{\Gamma(1 + j\beta + k\alpha)}. \quad (18c)$$

Proof Based on Theorem 1, we consider solutions of the form

$$y(t) = y_0 \sum_{j=0}^{\infty} \sum_{k=0}^j \tilde{\theta}_{j,k} t^{j\beta + k\alpha},$$

where $\tilde{\theta}_{0,0} = 1$ in order to satisfy the initial condition. Introduced in the problem equation, it yields

$$y_0 \sum_{j=1}^{\infty} \sum_{k=0}^j \frac{\Gamma(1 + j\beta + k\alpha)}{\Gamma(1 + (j-1)\beta + k\alpha)} \tilde{\theta}_{j,k} t^{(j-1)\beta + k\alpha} = y_0 \left(\mu \sum_{j=0}^{\infty} \sum_{k=0}^j \tilde{\theta}_{j,k} t^{j\beta + k\alpha} + \lambda \sum_{j=0}^{\infty} \sum_{k=0}^j \tilde{\theta}_{j,k} t^{j\beta + (k+1)\alpha} \right).$$

By reorganising the summation indexes, one gets

$$\sum_{j=0}^{\infty} \left(\sum_{k=0}^{j+1} \frac{\Gamma(1 + (j+1)\beta + k\alpha)}{\Gamma(1 + j\beta + k\alpha)} \tilde{\theta}_{j+1,k} - \lambda \sum_{k=1}^{j+1} \tilde{\theta}_{j,k-1} - \mu \sum_{k=0}^j \tilde{\theta}_{j,k} \right) t^{j\beta + k\alpha} = 0,$$

and from the term in brackets

$$\begin{aligned} & \frac{\Gamma(1 + (j+1)\beta)}{\Gamma(1 + j\beta)} \tilde{\theta}_{j+1,0} - \mu \tilde{\theta}_{j,0} + \\ & \frac{\Gamma(1 + (j+1)\beta + (j+1)\alpha)}{\Gamma(1 + j\beta + (j+1)\alpha)} \tilde{\theta}_{j+1,j+1} - \lambda \tilde{\theta}_{j,j} + \\ & \sum_{k=1}^j \left(\frac{\Gamma(1 + (j+1)\beta + k\alpha)}{\Gamma(1 + j\beta + k\alpha)} \tilde{\theta}_{j+1,k} - \lambda \tilde{\theta}_{j,k-1} - \mu \tilde{\theta}_{j,k} \right) = 0, \end{aligned}$$

resulting in the following recursion relations

$$\begin{aligned} \tilde{\theta}_{j,0} &= \mu \frac{\Gamma(1 + (j-1)\beta)}{\Gamma(1 + j\beta)} \tilde{\theta}_{j-1,0}, & j \geq 1 \\ \tilde{\theta}_{j,j} &= \lambda \frac{\Gamma(1 + (j-1)\beta + j\alpha)}{\Gamma(1 + j\beta + j\alpha)} \tilde{\theta}_{j-1,j-1}, & j \geq 1 \\ \tilde{\theta}_{j,k} &= \frac{\Gamma(1 + (j-1)\beta + k\alpha)}{\Gamma(1 + j\beta + k\alpha)} (\lambda \tilde{\theta}_{j-1,k-1} + \mu \tilde{\theta}_{j-1,k}), & 1 \leq k < j. \end{aligned}$$

By defining the factors $\rho_{j,k} = \frac{\Gamma(1 + (j-1)\beta + k\alpha)}{\Gamma(1 + j\beta + k\alpha)}$, the coefficients $\tilde{\theta}_{j,k}$ can be rewritten by recursion as

$$\begin{aligned} \tilde{\theta}_{j,0} &= \mu^j \theta_{j,0}, & \theta_{j,0} &= \rho_{j,0} \theta_{j-1,0}, & j \geq 1 \\ \tilde{\theta}_{j,j} &= \lambda^j \theta_{j,j}, & \theta_{j,j} &= \rho_{j,j} \theta_{j-1,j-1}, & j \geq 1 \\ \tilde{\theta}_{j,k} &= \mu^{j-k} \lambda^k \theta_{j,k}, & \theta_{j,k} &= \rho_{j,k} (\theta_{j-1,k-1} + \theta_{j-1,k}), & 1 \leq k < j \end{aligned}$$

where coefficients $\theta_{j,j}$ agree with those by Theorem 1 with $\theta_{j,j} = \theta_j$, and $\theta_{j,0} = \frac{1}{\Gamma(1+\beta j)}$ coincide with the coefficients of the Mittag–Leffler function, which completes the proof. \square

To improve clarity, the structure of the coefficients $\theta_{j,k}$ and their associated monomial terms are illustrated in Figure 2. From this figure, it is easy to see that the solution can be also rewritten as an alternative series expansion through its main diagonals, in the form of

$$y(t) = y_0 \sum_{j=0}^{\infty} \sum_{k=0}^j \mu^{j-k} \lambda^k \theta_{j,k} t^{j\beta + k\alpha} = y_0 \sum_{n=0}^{\infty} \sum_{k=0}^{\infty} \mu^n \lambda^k \theta_{n+k,k} t^{n\beta} t^{k(\alpha+\beta)} = y_0 \sum_{n=0}^{\infty} (\mu t^\beta)^n \sum_{k=0}^{\infty} \theta_{n+k,k} (\lambda t^{\alpha+\beta})^k,$$

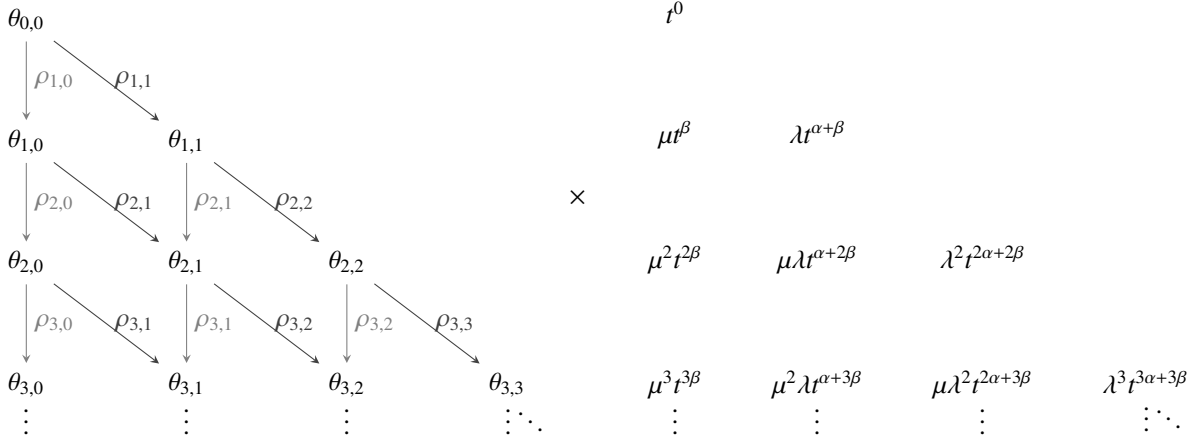


Figure 2: Structure of coefficients and associated monomial terms in the solution of $\partial_t^\beta y = (\mu + \lambda t^\alpha)y$.

where n indicates the diagonal number. For $\beta = 1$, the recursion relations in (18b) become $\theta_{j,k} = \frac{1}{(j-k)! k! (1+\alpha)^k}$, and therefore

$$y(t) = y_0 \sum_{n=0}^{\infty} (\mu t)^n \sum_{k=0}^{\infty} \theta_{n+k,k} (\lambda t^{1+\alpha})^k = y_0 \sum_{n=0}^{\infty} \frac{(\mu t)^n}{n!} \sum_{k=0}^{\infty} \frac{1}{k!} \left(\frac{\lambda t^{1+\alpha}}{1+\alpha} \right)^k = y_0 \exp \left(\mu t + \lambda \frac{t^{1+\alpha}}{1+\alpha} \right),$$

which is the expected solution to $\partial_t y = (\mu + \lambda t^\alpha)y$, $y(t_0) = y_0$, in the standard diffusion in time case.

Theorem 3 (Subproblem (15c), $\mu = 0$). *The solution of $\partial_t^\beta y = \lambda(\delta - t)^\alpha y$, $y(0) = y_0$, is given by*

$$y(t) = y_0 \left(1 + \sum_{j=1}^{\infty} \frac{(\lambda \delta^\alpha t^\beta)^j}{\Gamma(1+j\beta)} f_B(\{a_j\}, \{b_j\}; 1+j\beta; \frac{t}{\delta}) \right) \quad (21a)$$

with $\{a_j\} = \{1, 1+\beta+n_1, \dots, 1+(j-1)\beta+n_1+\dots+n_{j-1}\}$, $\{b_j\} = -\alpha \mathbf{1}_j$, where $\mathbf{1}_j$ is the vector of ones of length j , and $f_B(\{a_j\}, \{b_j\}; c; \{z_j\})$ is the Lauricella function of the second kind [22, pp. 58-59]

$$f_B(\{a_j\}, \{b_j\}; c; \{z_j\}) = \sum_{n_1, \dots, n_j=0}^{\infty} \frac{(a_1)_{n_1} \dots (a_j)_{n_j} (b_1)_{n_1} \dots (b_j)_{n_j}}{(c)_{n_1+\dots+n_j}} \frac{z_1^{n_1} \dots z_j^{n_j}}{n_1! \dots n_j!}, \quad (21b)$$

and $(z)_n = z(z+1) \dots (z+n-1) = \Gamma(z+n)/\Gamma(z)$ denotes the Pochhammer symbol.

Proof For $0 < \beta \leq 1$, the Cauchy problem for the fractional differential equation $\partial_t^\beta y = \lambda(\delta - t)^\alpha y$ is equivalent to the solution of the Volterra integral equation of the second kind of the form [20, pp. 230-231]

$$y(t) = y_0 + \frac{\lambda}{\Gamma(\beta)} \int_0^t \frac{(\delta-s)^\alpha}{(t-s)^{1-\beta}} y(s) ds,$$

which can be approached by the method of successive approximations [20, pp. 230-231]). By defining the linear operator

$$\mathcal{A}\{f\}(t) = \frac{\lambda}{\Gamma(\beta)} \int_0^t \frac{(\delta-s)^\alpha}{(t-s)^{1-\beta}} f(s) ds,$$

and expressing the solution as $y(t) = \sum_{j=0}^{\infty} y_j(t)$, $y_0(t) = y_0$, then each of the $y_j(t)$ terms satisfies

$$y_j(t) = \mathcal{A}\{y_{j-1}\}(t).$$

For $j = 1$, and using the change of variable $s = tx$, this yields

$$\begin{aligned} y_1(t) &= y_0 \frac{\lambda}{\Gamma(\beta)} \int_0^t \frac{(\delta - s)^\alpha}{(t - s)^{1-\beta}} ds = y_0 \frac{\lambda}{\Gamma(\beta)} \int_0^1 (t - tx)^{\beta-1} (\delta - tx)^\alpha t dx = \\ &= y_0 \frac{\lambda \delta^\alpha t^\beta}{\Gamma(\beta)} \int_0^1 (1 - x)^{\beta-1} \left(1 - \frac{t}{\delta} x\right)^\alpha dx = y_0 \frac{\lambda \delta^\alpha t^\beta}{\Gamma(1 + \beta)} {}_2F_1\left(1, -\alpha; 1 + \beta; \frac{t}{\delta}\right), \end{aligned}$$

where the Euler integral representation of the Gauss hypergeometric function has been used

$${}_2F_1(a, b; c; z) = f_B(a, b; c; z) = \sum_{n=0}^{\infty} \frac{(a)_n (b)_n}{(c)_n} \frac{z^n}{n!} = \frac{\Gamma(c)}{\Gamma(a)\Gamma(c-a)} \int_0^1 x^{a-1} (1-x)^{c-a-1} (1-zx)^{-b} dx.$$

For $j = 2$, and using the identities $\Gamma(z+n) = (z)_n \Gamma(z)$ and $(z)_{n_1+\dots+n_j}(z+n_1+\dots+n_j) = (z)_{n_1+\dots+n_j}$ to simplify terms, we get

$$\begin{aligned} y_2(t) &= y_0 \frac{\lambda^2 \delta^\alpha}{\Gamma(\beta)\Gamma(1+\beta)} \sum_{n_1=0}^{\infty} \frac{(1)_{n_1}(-\alpha)_{n_1}}{(1+\beta)_{n_1} n_1! \delta^{n_1}} \int_0^t s^{\beta+n_1} (t-s)^{\beta-1} (\delta-s)^\alpha ds = \\ &= y_0 \frac{(\lambda \delta^\alpha t^\beta)^2}{\Gamma(\beta)\Gamma(1+\beta)} \sum_{n_1=0}^{\infty} \left(\frac{t}{\delta}\right)^{n_1} \frac{(1)_{n_1}(-\alpha)_{n_1}}{(1+\beta)_{n_1} n_1!} \int_0^1 x^{\beta+n_1} (1-x)^{\beta-1} \left(1 - \frac{t}{\delta} x\right)^\alpha dx = \\ &= y_0 \frac{(\lambda \delta^\alpha t^\beta)^2}{\Gamma(\beta)\Gamma(1+\beta)} \sum_{n_1=0}^{\infty} \left(\frac{t}{\delta}\right)^{n_1} \frac{(1)_{n_1}(-\alpha)_{n_1}}{(1+\beta)_{n_1} n_1!} \frac{\Gamma(1+\beta+n_1)\Gamma(\beta)}{\Gamma(1+2\beta+n_1)} {}_2F_1\left(1+\beta+n_1, -\alpha; 1+2\beta+n_1; \frac{t}{\delta}\right) = \\ &= y_0 \frac{(\lambda \delta^\alpha t^\beta)^2}{\Gamma(1+2\beta)} \sum_{n_1=0}^{\infty} \left(\frac{t}{\delta}\right)^{n_1} \frac{(1)_{n_1}(-\alpha)_{n_1}}{(1+2\beta)_{n_1} n_1!} {}_2F_1\left(1+\beta+n_1, -\alpha; 1+2\beta+n_1; \frac{t}{\delta}\right) = \\ &= y_0 \frac{(\lambda \delta^\alpha t^\beta)^2}{\Gamma(1+2\beta)} \sum_{n_1, n_2=0}^{\infty} \left(\frac{t}{\delta}\right)^{n_1+n_2} \frac{(1)_{n_1}(1+\beta+n_1)_{n_2}(-\alpha)_{n_1}(-\alpha)_{n_2}}{(1+2\beta)_{n_1+n_2} n_1! n_2!} = \\ &= y_0 \frac{(\lambda \delta^\alpha t^\beta)^2}{\Gamma(1+2\beta)} f_B\left(1, 1+\beta+n_1, -\alpha, -\alpha; 1+2\beta; \frac{t}{\delta}\right). \end{aligned}$$

The remaining terms involve integrals of the form

$$\begin{aligned} \mathcal{A}\left\{\frac{t^{j\beta}}{\Gamma(1+j\beta)} f_B\left(\{a_j\}, \{b_j\}; 1+j\beta; \frac{t}{\delta}\right)\right\}(t) &= \\ &= \frac{\lambda}{\Gamma(\beta)\Gamma(1+j\beta)} \sum_{n_1, \dots, n_j=0}^{\infty} \frac{(a_1)_{n_1} \dots (a_j)_{n_j} (b_1)_{n_1} \dots (b_j)_{n_j}}{(1+j\beta)_{n_1+\dots+n_j} n_1! \dots n_j! \delta^{n_1+\dots+n_j}} \int_0^t s^{j\beta+n_1+\dots+n_j} (t-s)^{\beta-1} (\delta-s)^\alpha ds = \\ &= \frac{\lambda \delta^\alpha t^{(j+1)\beta}}{\Gamma(\beta)\Gamma(1+j\beta)} \sum_{n_1, \dots, n_j=0}^{\infty} \left(\frac{t}{\delta}\right)^{n_1+\dots+n_j} \frac{(a_1)_{n_1} \dots (a_j)_{n_j} (b_1)_{n_1} \dots (b_j)_{n_j}}{(1+j\beta)_{n_1+\dots+n_j} n_1! \dots n_j!} \int_0^1 x^{j\beta+n_1+\dots+n_j} (1-x)^{\beta-1} \left(1 - \frac{t}{\delta} x\right)^\alpha dx = \\ &= \frac{\lambda \delta^\alpha t^{(j+1)\beta}}{\Gamma(\beta)\Gamma(1+j\beta)} \sum_{n_1, \dots, n_j=0}^{\infty} \left(\frac{t}{\delta}\right)^{n_1+\dots+n_j} \frac{(a_1)_{n_1} \dots (a_j)_{n_j} (b_1)_{n_1} \dots (b_j)_{n_j}}{(1+j\beta)_{n_1+\dots+n_j} n_1! \dots n_j!} \times \\ &\quad \times \frac{\Gamma(1+j\beta+n_1+\dots+n_j)\Gamma(\beta)}{\Gamma(1+(j+1)\beta+n_1+\dots+n_j)} {}_2F_1\left(1+j\beta+n_1+\dots+n_j, -\alpha; 1+(j+1)\beta+n_1+\dots+n_j, \frac{t}{\delta}\right) = \\ &= \frac{\lambda \delta^\alpha t^{(j+1)\beta}}{\Gamma(1+(j+1)\beta)} \sum_{n_1, \dots, n_{j+1}=0}^{\infty} \left(\frac{t}{\delta}\right)^{n_1+\dots+n_{j+1}} \frac{(a_1)_{n_1} \dots (a_j)_{n_j} (1+j\beta+n_1+\dots+n_j)_{n_{j+1}} (b_1)_{n_1} \dots (b_j)_{n_j} (-\alpha)_{n_{j+1}}}{(1+(j+1)\beta)_{n_1+\dots+n_{j+1}} n_1! \dots n_{j+1}!} = \\ &= \frac{\lambda \delta^\alpha t^{(j+1)\beta}}{\Gamma(1+(j+1)\beta)} f_B\left(\{a_j, 1+j\beta+n_1+\dots+n_j\}, \{b_j, -\alpha\}; 1+(j+1)\beta; \frac{t}{\delta}\right), \end{aligned}$$

where $a_{j+1} = 1 + j\beta + n_1 + \dots + n_j$, $b_{j+1} = -\alpha$. The application of \mathcal{A} to the $y_j(t)$ terms therefore results in their multiplication by the factor $\lambda \delta^\alpha t^\beta \frac{\Gamma(1+j\beta)}{\Gamma(1+(j+1)\beta)}$, the increase of order of coefficients $\{a_j\}$ and $\{b_j\}$ in their Lauricella function to $\{a_j, 1 + j\beta + n_1 + \dots + n_j\}$ and $\{b_j, -\alpha\}$, respectively, and an increase by β of coefficient c , which provides the general form of solution (21a). \square

Corollary 1. The solution of $\partial_t^\beta y = \lambda(\delta - t)^\alpha y$, $y(0) = y_0$, at $t = \delta$ is

$$y(\delta) = y_0 \sum_{j=0}^{\infty} \xi_j (\lambda \delta^{\alpha+\beta})^j, \quad (22a)$$

with coefficients ξ_j given by

$$\xi_j = \frac{\Gamma(1 + (j-1)(\alpha + \beta))}{\Gamma(1 + j(\alpha + \beta))} \frac{\Gamma(j(\alpha + \beta))}{\Gamma(j(\alpha + \beta) - \alpha)} \xi_{j-1}, \quad \xi_0 = 1. \quad (22b)$$

Proof The result arises from recursively considering each of the nested parts of the Lauricella functions $y_j(t)$ as a Gauss hypergeometric function evaluated at $t/\delta = 1$, which satisfies [20, pp. 27-28]

$${}_2F_1(a, b; c; 1) = \frac{\Gamma(c)\Gamma(c-a-b)}{\Gamma(c-a)\Gamma(c-b)}.$$

Hence, recalling that $\{a_j\} = \{1, 1 + \beta + n_1, \dots, 1 + (j-1)\beta + n_1 + \dots + n_{j-1}\}$, $\{b_j\} = -\alpha \vec{1}_j$, $c = 1 + j\beta$, after j iterations of recursion we get

$$\begin{aligned} y_j(\delta) &= \frac{(\lambda \delta^{\alpha+\beta})^j}{\Gamma(1 + j\beta)} \sum_{n_1, \dots, n_{j-1}=0}^{\infty} \frac{(a_1)_{n_1} \dots (a_{j-1})_{n_{j-1}} (b_1)_{n_1} \dots (b_{j-1})_{n_{j-1}}}{(1 + j\beta)_{n_1 + \dots + n_{j-1}} n_1! \dots n_{j-1}!} \times \\ &\quad \times {}_2F_1(1 + (j-1)\beta + n_1 + \dots + n_{j-1}, -\alpha; 1 + j\beta + n_1 + \dots + n_{j-1}; 1) = \\ &= \frac{(\lambda \delta^{\alpha+\beta})^j}{\Gamma(1 + j\beta)} \sum_{n_1, \dots, n_{j-1}=0}^{\infty} \frac{(a_1)_{n_1} \dots (a_{j-1})_{n_{j-1}} (b_1)_{n_1} \dots (b_{j-1})_{n_{j-1}}}{(1 + j\beta)_{n_1 + \dots + n_{j-1}} n_1! \dots n_{j-1}!} \frac{(1 + j\beta)_{n_1 + \dots + n_{j-1}} \Gamma(1 + j\beta) \Gamma(\alpha + \beta)}{\Gamma(\beta) (1 + \alpha + j\beta)_{n_1 + \dots + n_{j-1}} \Gamma(1 + \alpha + j\beta)} = \\ &= \frac{(\lambda \delta^{\alpha+\beta})^j}{\Gamma(1 + \alpha + j\beta)} \frac{\Gamma(\alpha + \beta)}{\Gamma(\beta)} \sum_{n_1, \dots, n_{j-2}=0}^{\infty} \frac{(a_1)_{n_1} \dots (a_{j-2})_{n_{j-2}} (b_1)_{n_1} \dots (b_{j-2})_{n_{j-2}}}{(1 + \alpha + j\beta)_{n_1 + \dots + n_{j-2}} n_1! \dots n_{j-2}!} \times \\ &\quad \times {}_2F_1(1 + (j-2)\beta + n_1 + \dots + n_{j-2}, -\alpha; 1 + \alpha + j\beta + n_1 + \dots + n_{j-2}; 1) = \\ &= \frac{(\lambda \delta^{\alpha+\beta})^j}{\Gamma(1 + 2\alpha + j\beta)} \frac{\Gamma(\alpha + \beta)}{\Gamma(\beta)} \frac{\Gamma(2\alpha + 2\beta)}{\Gamma(\alpha + 2\beta)} \sum_{n_1, \dots, n_{j-3}=0}^{\infty} \frac{(a_1)_{n_1} \dots (a_{j-3})_{n_{j-3}} (b_1)_{n_1} \dots (b_{j-3})_{n_{j-3}}}{(1 + 2\alpha + j\beta)_{n_1 + \dots + n_{j-3}} n_1! \dots n_{j-3}!} \times \\ &\quad \times {}_2F_1(1 + (j-3)\beta + n_1 + \dots + n_{j-3}, -\alpha; 1 + 2\alpha + j\beta + n_1 + \dots + n_{j-3}; 1) = \dots = \\ &= \frac{(\lambda \delta^{\alpha+\beta})^j}{\Gamma(1 + j(\alpha + \beta))} \prod_{n=1}^j \frac{\Gamma(n(\alpha + \beta))}{\Gamma(n(\alpha + \beta) - \alpha)}. \end{aligned}$$

From here,

$$\frac{y_j(\delta)}{y_{j-1}(\delta)} = \lambda \delta^{\alpha+\beta} \frac{\Gamma(1 + (j-1)(\alpha + \beta))}{\Gamma(1 + j(\alpha + \beta))} \frac{\Gamma(j(\alpha + \beta))}{\Gamma(j(\alpha + \beta) - \alpha)}.$$

The definition of coefficients ξ_j as given by (22b) completes the proof. \square

For $\beta = 1$, coefficients $\xi_j = \frac{1}{j(1+\alpha)} \xi_{j-1} = \frac{1}{j!(1+\alpha)^j}$, and therefore

$$y(\delta) = y_0 \sum_{j=0}^{\infty} \frac{1}{j!} \left(\lambda \frac{\delta^{1+\alpha}}{1+\alpha} \right)^j = y_0 \exp \left(\lambda \frac{\delta^{1+\alpha}}{1+\alpha} \right),$$

which is the expected solution at $t = \delta$ to $\partial_t y = \lambda(\delta - t)^\alpha y$, $y(t_0) = y_0$, in the standard diffusion in time case.

Theorem 4 (Subproblem (15c), $\mu \neq 0$). The solution of $\partial_t^\beta y = (-\mu + \lambda(\delta - t)^\alpha)y$, $y(0) = y_0$, is given by

$$y(t) = y_0 \left(E_\beta(-\mu t^\beta) + \sum_{j=1}^{\infty} \sum_{k=1}^j \frac{(-\mu)^{j-k} (\lambda \delta^\alpha)^k t^{j\beta}}{\Gamma(1 + j\beta)} \sum_{m=1}^p f_B \left(\{a_{j,k}^{(m)}\}, \{b_k\}; 1 + j\beta; \frac{t}{\delta} \right) \right) \quad (23a)$$

where $E_\beta(z)$ is the Mittag–Leffler function and $f_B \left(\{a_{j,k}^{(m)}\}, \{b_k\}; c; \{z_k\} \right)$ are Lauricella functions of the second kind, satisfying $\{b_k\} = -\alpha \vec{1}_k$ and

$$\{a_{j,k}^{(m)}\} = \{1 + \pi_{j,k}^{(m,1)} \beta, 1 + \pi_{j,k}^{(m,2)} \beta + n_1, \dots, 1 + \pi_{j,k}^{(m,k)} \beta + n_1 + \dots + n_{k-1}\}, \quad (23b)$$

where $\pi_{j,k}^{(m)}$ is the m -th of the $p = \binom{j}{k}$ strictly increasing partitions of size k of the set of integers $\{0, 1, \dots, j-1\}$, and $\pi_{j,k}^{(m,n)}$ denotes its n -th component.

Proof The solution of the Cauchy problem is given in this case by the Volterra integral equation of the form

$$y(t) = y_0 + \frac{\lambda}{\Gamma(\beta)} \int_0^t \frac{(\delta - s)^\alpha}{(t - s)^{1-\beta}} y(s) ds - \frac{\mu}{\Gamma(\beta)} \int_0^t \frac{y(s)}{(t - s)^{1-\beta}} ds.$$

By defining the linear operators

$$\mathcal{A}\{f\}(t) = \frac{\lambda}{\Gamma(\beta)} \int_0^t \frac{(\delta - s)^\alpha}{(t - s)^{1-\beta}} f(s) ds, \quad \mathcal{B}\{f\}(t) = -\frac{\mu}{\Gamma(\beta)} \int_0^t \frac{f(s)}{(t - s)^{1-\beta}} ds,$$

as well as solutions in the form of $y(t) = \sum_{j=0}^{\infty} \sum_{k=0}^j y_{j,k}(t)$, $y_{0,0}(t) = y_0$, then each $y_{j,k}(t)$ satisfies

$$y_{j,k}(t) = \mathcal{A}\{y_{j-1,k-1}\}(t) + \mathcal{B}\{y_{j-1,k}\}(t).$$

Note that this notation also reflects the structure of solutions previously highlighted in Figure 2, with \mathcal{A} representing the operator through the diagonals, and \mathcal{B} the vertical operator.

The operator \mathcal{A} was previously analysed in Theorem 3. In this case, it involves integrals of the form

$$\begin{aligned} \mathcal{A} \left\{ \frac{t^{j\beta}}{\Gamma(1 + j\beta)} f_B \left(\{a_{j,k}\}, \{b_k\}; 1 + j\beta; \frac{t}{\delta} \right) \right\} (t) &= \\ &= \frac{\lambda \delta^\alpha t^{(j+1)\beta}}{\Gamma(1 + (j+1)\beta)} f_B \left(\{a_{j,k}, 1 + j\beta + n_1 + \dots + n_k\}, \{b_k, -\alpha\}; 1 + (j+1)\beta; \frac{t}{\delta} \right), \end{aligned}$$

which follows from the application of the same principles. Its action therefore results in the multiplication by the factor $\lambda \delta^\alpha t^\beta \frac{\Gamma(1+j\beta)}{\Gamma(1+(j+1)\beta)}$, an increase in order of coefficients $\{a_{j,k}\}$ and $\{b_k\}$ to $\{a_{j,k}, 1 + j\beta + n_1 + \dots + n_k\}$ and $\{b_k, -\alpha\}$, respectively, and the increase by β of coefficient c .

From the definition of \mathcal{B} , it is immediate to observe that its application to the $y_{j,0}(t)$ terms coincides with the series expansion of the one-parametric Mittag–Leffler function $E_\beta(-\mu t^\beta)$. The application of \mathcal{B} to the rest of $y_{j,k}(t)$ terms, given the nature of the $y_{j,j}(t)$ terms in the first diagonal as provided by (21a), involves integrals of the form

$$\begin{aligned} \mathcal{B} \left\{ \frac{t^{j\beta}}{\Gamma(1 + j\beta)} f_B \left(\{a_{j,k}\}, \{b_k\}; 1 + j\beta; \frac{t}{\delta} \right) \right\} (t) &= \\ &= -\frac{\mu}{\Gamma(\beta)\Gamma(1 + j\beta)} \sum_{n_1, \dots, n_k=0}^{\infty} \frac{(a_1)_{n_1} \dots (a_k)_{n_k} (b_1)_{n_1} \dots (b_k)_{n_k}}{(1 + j\beta)_{n_1 + \dots + n_k} n_1! \dots n_k! \delta^{n_1 + \dots + n_k}} \int_0^t s^{j\beta + n_1 + \dots + n_k} (t - s)^{\beta-1} ds = \\ &= -\frac{\mu t^{(j+1)\beta}}{\Gamma(\beta)\Gamma(1 + j\beta)} \sum_{n_1, \dots, n_k=0}^{\infty} \left(\frac{t}{\delta} \right)^{n_1 + \dots + n_k} \frac{(a_1)_{n_1} \dots (a_k)_{n_k} (b_1)_{n_1} \dots (b_k)_{n_k}}{(1 + j\beta)_{n_1 + \dots + n_k} n_1! \dots n_k!} \int_0^1 x^{j\beta + n_1 + \dots + n_k} (1 - x)^{\beta-1} dx = \\ &= -\frac{\mu t^{(j+1)\beta}}{\Gamma(\beta)\Gamma(1 + j\beta)} \sum_{n_1, \dots, n_k=0}^{\infty} \left(\frac{t}{\delta} \right)^{n_1 + \dots + n_k} \frac{(a_1)_{n_1} \dots (a_k)_{n_k} (b_1)_{n_1} \dots (b_k)_{n_k}}{(1 + j\beta)_{n_1 + \dots + n_k} n_1! \dots n_k!} \frac{\Gamma(1 + j\beta + n_1 + \dots + n_k) \Gamma(\beta)}{\Gamma(1 + (j+1)\beta + n_1 + \dots + n_k)} = \end{aligned}$$

$$\begin{aligned}
&= -\frac{\mu t^{(j+1)\beta}}{\Gamma(1+(j+1)\beta)} \sum_{n_1, \dots, n_k=0}^{\infty} \left(\frac{t}{\delta}\right)^{n_1+\dots+n_k} \frac{(a_1)_{n_1} \dots (a_k)_{n_k} (b_1)_{n_1} \dots (b_k)_{n_k}}{(1+(j+1)\beta)_{n_1+\dots+n_k} n_1! \dots n_k!} = \\
&= -\frac{\mu t^{(j+1)\beta}}{\Gamma(1+(j+1)\beta)} f_B\left(\{a_{j,k}\}, \{b_k\}; 1+(j+1)\beta; \frac{t}{\delta}\right),
\end{aligned}$$

where the change of variable $s = tx$ and the definition of the Beta function

$$B(z, w) = \int_0^1 x^{z-1} (1-x)^{w-1} dx = \frac{\Gamma(z)\Gamma(w)}{\Gamma(z+w)}$$

have been used. The application of \mathcal{B} therefore results in the multiplication by $-\mu t^\beta \frac{\Gamma(1+j\beta)}{\Gamma(1+(j+1)\beta)}$ and an increase by β of the coefficient c in the Lauricella functions, leaving unaffected the sets of coefficients $\{a_{j,k}\}$ and $\{b_k\}$.

As a result of descending through the solution tree, each $y_{j,k}(t)$ is given by the summation of $p_{\mathcal{A}} = \binom{j-1}{k-1}$ and $p_{\mathcal{B}} = \binom{j-1}{k}$ terms, therefore satisfying $p = \binom{j-1}{k-1} + \binom{j-1}{k} = \binom{j}{k}$ (Pascal's identity). The number of times that the previous terms have been multiplied by $(-\mu)$ corresponds to the difference of the numerator and the denominator of their respective binomials, whereas the powers of λ are given by the binomial's denominators. Thus,

$$\begin{aligned}
y_{j,k}(t) &= \mathcal{A}\{y_{j-1,k-1}\}(t) + \mathcal{B}\{y_{j-1,k}\}(t) = \\
&= \sum_{m=1}^{p_{\mathcal{A}}} \mathcal{A}\left\{\frac{(-\mu)^{j-k}(\lambda\delta^\alpha)^{k-1}t^{(j-1)\beta}}{\Gamma(1+(j-1)\beta)} f_B\left(\{a_{j-1,k-1}^{(m)}\}, \{b_{k-1}\}; 1+(j-1)\beta; \frac{t}{\delta}\right)\right\}(t) + \\
&+ \sum_{m=1}^{p_{\mathcal{B}}} \mathcal{B}\left\{\frac{(-\mu)^{j-k-1}(\lambda\delta^\alpha)^k t^{(j-1)\beta}}{\Gamma(1+(j-1)\beta)} f_B\left(\{a_{j-1,k}^{(m)}\}, \{b_k\}; 1+(j-1)\beta; \frac{t}{\delta}\right)\right\}(t) = \\
&= \frac{(-\mu)^{j-k}(\lambda\delta^\alpha)^k t^{j\beta}}{\Gamma(1+j\beta)} \sum_{m=1}^{p_{\mathcal{A}}} f_B\left(\{a_{j-1,k-1}^{(m)}\}, 1+(j-1)\beta+n_1+\dots+n_k, \{b_k\}; 1+j\beta; \frac{t}{\delta}\right) + \\
&+ \frac{(-\mu)^{j-k}(\lambda\delta^\alpha)^k t^{j\beta}}{\Gamma(1+j\beta)} \sum_{m=1}^{p_{\mathcal{B}}} f_B\left(\{a_{j-1,k}^{(m)}\}, \{b_k\}; 1+j\beta; \frac{t}{\delta}\right) = \\
&= \frac{(-\mu)^{j-k}(\lambda\delta^\alpha)^k t^{j\beta}}{\Gamma(1+j\beta)} \sum_{m=1}^p f_B\left(\{a_{j,k}^{(m)}\}, \{b_k\}; 1+j\beta; \frac{t}{\delta}\right),
\end{aligned}$$

where by noting that $\{a_{j,k}\} = \{a_{j-1,k-1}, 1+(j-1)\beta+n_1+\dots+n_k\} \cup \{a_{j-1,k}\}$, or equivalently $\pi_{j,k} = \{\pi_{j-1,k-1}, j-1\} \cup \pi_{j-1,k}$ given their correspondence, completes the proof. \square

To improve the clarity of notation, the partitions $\pi_{j,k}^{(m)}$ and the resulting coefficients $\{a_{j,k}^{(m)}\}$ associated with the terms of the solution are presented up to $j = 3$ in Table 1.

Corollary 2. The solution of $\partial_t^\beta y = (-\mu + \lambda(\delta - t)^\alpha)y$, $y(0) = y_0$, at $t = \delta$ is

$$y(\delta) = y_0 \sum_{j=0}^{\infty} \sum_{k=0}^j (-\mu)^{j-k} \lambda^k \xi_{j,k} \delta^{j\beta+k\alpha} \quad (24a)$$

with coefficients $\xi_{j,k}$ given by

$$\xi_{j,j} = \hat{\rho}_{j,j} \xi_{j-1,j-1} \quad (j \geq 1), \quad \xi_{j,k} = \hat{\rho}_{j,k} \xi_{j-1,k-1} + \hat{\sigma}_{j,k} \xi_{j-1,k} \quad (1 \leq k < j), \quad \xi_{j,0} = \frac{1}{\Gamma(1+j\beta)}, \quad (24b)$$

where the multiplicative factors $\hat{\rho}_{j,k}$ and $\hat{\sigma}_{j,k}$ are defined as

$$\hat{\rho}_{j,k} = \frac{\Gamma(1+(j-1)\beta + (k-1)\alpha)}{\Gamma(1+j\beta + k\alpha)} \frac{\Gamma(j\beta + k\alpha)}{\Gamma(j\beta + (k-1)\alpha)}, \quad \hat{\sigma}_{j,k} = \frac{\Gamma(1+(j-1)\beta + k\alpha)}{\Gamma(1+j\beta + k\alpha)}. \quad (24c)$$

j	k	m	$\pi_{j,k}^{(m)}$	$\{a_{j,k}^{(m)}\}$
1	1	1	{0}	{1}
2	1	1	{0}	{1}
		2	{1}	{1+ β }
3	2	1	{0,1}	{1,1+ β + n_1 }
		1	{0}	{1}
		2	{1}	{1+ β }
	2	3	{2}	{1+2 β }
		1	{0,1}	{1,1+ β + n_1 }
		2	{0,2}	{1,1+2 β + n_1 }
		3	{1,2}	{1+ β ,1+2 β + n_1 }
	3	1	{0,1,2}	{1,1+ β + n_1 ,1+2 β + n_1 + n_2 }

Table 1: Strictly increasing partitions $\pi_{j,k}^{(m)}$ of size k of the set of integers $\{0, 1, \dots, j-1\}$ and associated coefficients $\{a_{j,k}^{(m)}\}$ in the structure of the solution of $\partial_t^2 y = (-\mu + \lambda(\delta - t)^\alpha)y$.

Proof The result newly arises from recursively considering each of the nested parts of the Lauricella functions $y_{j,k}(t)$ as a Gauss hypergeometric function evaluated at $t/\delta = 1$. Recalling that in this case

$$\{a_{j,k}^{(m)}\} = \{1 + \pi_{j,k}^{(m,1)}\beta, 1 + \pi_{j,k}^{(m,2)}\beta + n_1, \dots, 1 + \pi_{j,k}^{(m,k)}\beta + n_1 + \dots + n_{k-1}\},$$

$\{b_k\} = -\alpha \vec{\mathbf{1}}_k$, $c = 1 + j\beta$, and calling for simplicity of notation a_n and π_n to the n -th components of sets $\{a_{j,k}^{(m)}\}$ and $\{\pi_{j,k}^{(m)}\}$, then for each $y_{j,k}^{(m)}(t)$ in the $p = \binom{j}{k}$ Lauricella functions, after k recursions we get

$$\begin{aligned}
y_{j,k}^{(m)}(\delta) &= \frac{(-\mu)^{j-k} \lambda^k \delta^{j\beta+k\alpha}}{\Gamma(1+j\beta)} \sum_{n_1, \dots, n_{k-1}=0}^{\infty} \frac{(a_1)_{n_1} \cdots (a_{k-1})_{n_{k-1}} (b_1)_{n_1} \cdots (b_{k-1})_{n_{k-1}}}{(1+j\beta)_{n_1+\dots+n_{k-1}} n_1! \cdots n_{k-1}!} \times \\
&\quad \times {}_2F_1(1 + \pi_k \beta + n_1 + \dots + n_{k-1}, -\alpha; 1 + j\beta + n_1 + \dots + n_{k-1}; 1) = \\
&= \frac{(-\mu)^{j-k} \lambda^k \delta^{j\beta+k\alpha}}{\Gamma(1+j\beta)} \sum_{n_1, \dots, n_{k-1}=0}^{\infty} \frac{(a_1)_{n_1} \cdots (a_{k-1})_{n_{k-1}} (b_1)_{n_1} \cdots (b_{k-1})_{n_{k-1}}}{(1+j\beta)_{n_1+\dots+n_{k-1}} n_1! \cdots n_{k-1}!} \times \\
&\quad \times \frac{(1+j\beta)_{n_1+\dots+n_{k-1}} \Gamma(1+j\beta) \Gamma(\alpha + (j - \pi_k)\beta)}{\Gamma((j - \pi_k)\beta) (1 + \alpha + j\beta)_{n_1+\dots+n_{k-1}} \Gamma(1 + \alpha + j\beta)} = \\
&= \frac{(-\mu)^{j-k} \lambda^k \delta^{j\beta+k\alpha}}{\Gamma(1 + \alpha + j\beta)} \frac{\Gamma(\alpha + (j - \pi_k)\beta)}{\Gamma((j - \pi_k)\beta)} \sum_{n_1, \dots, n_{k-2}=0}^{\infty} \frac{(a_1)_{n_1} \cdots (a_{k-2})_{n_{k-2}} (b_1)_{n_1} \cdots (b_{k-2})_{n_{k-2}}}{(1 + \alpha + j\beta)_{n_1+\dots+n_{k-2}} n_1! \cdots n_{k-2}!} \times \\
&\quad \times {}_2F_1(1 + \pi_{k-1} \beta + n_1 + \dots + n_{k-2}, -\alpha; 1 + \alpha + j\beta + n_1 + \dots + n_{k-2}; 1) = \\
&= \frac{(-\mu)^{j-k} \lambda^k \delta^{j\beta+k\alpha}}{\Gamma(1 + 2\alpha + j\beta)} \frac{\Gamma(\alpha + (j - \pi_k)\beta)}{\Gamma((j - \pi_k)\beta)} \frac{\Gamma(2\alpha + (j - \pi_{k-1})\beta)}{\Gamma(\alpha + (j - \pi_{k-1})\beta)} \sum_{n_1, \dots, n_{k-3}=0}^{\infty} \frac{(a_1)_{n_1} \cdots (a_{k-3})_{n_{k-3}} (b_1)_{n_1} \cdots (b_{k-3})_{n_{k-3}}}{(1 + 2\alpha + j\beta)_{n_1+\dots+n_{k-3}} n_1! \cdots n_{k-3}!} \times \\
&\quad \times {}_2F_1(1 + \pi_{k-2} \beta + n_1 + \dots + n_{k-3}, -\alpha; 1 + 2\alpha + j\beta + n_1 + \dots + n_{k-3}; 1) = \dots = \\
&= \frac{(-\mu)^{j-k} \lambda^k \delta^{j\beta+k\alpha}}{\Gamma(1 + j\beta + k\alpha)} \prod_{n=1}^k \frac{\Gamma(n\alpha + (j - \pi_{k-n+1})\beta)}{\Gamma(n\alpha + (j - \pi_{k-n+1})\beta - \alpha)}.
\end{aligned}$$

From the application of the formula above to the $y_{j,k}(t) = \sum_m^p y_{j,k}^{(m)}$ terms, $1 \leq k < j$, with $y_{j,0} = \frac{(-\mu\delta^\beta)^j}{\Gamma(1+j\beta)}$ and $y_{j,j}(\delta) = y_j(\delta)$ as given by (22a), then

$$y_{j,k}(\delta) = \lambda \delta^{\alpha+\beta} \frac{\Gamma(1 + (j-1)\beta + (k-1)\alpha)}{\Gamma(1 + j\beta + k\alpha)} \frac{\Gamma(j\beta + k\alpha)}{\Gamma(j\beta + (k-1)\alpha)} y_{j-1,k-1}(\delta) - \mu \delta^\beta \frac{\Gamma(1 + (j-1)\beta + k\alpha)}{\Gamma(1 + j\beta + k\alpha)} y_{j-1,k}(\delta),$$

where recursion in the powers of parameters μ and λ , and the definition of the multiplicative factors $\hat{\rho}_{j,k}$ and $\hat{\sigma}_{j,k}$ as given by (24c), completes the proof. \square

For $\beta = 1$, the algebraic manipulation of the resulting Gamma functions yields $\xi_{j,k} = \frac{1}{(j-k)!k!(1+\alpha)^k}$, and therefore

$$y(\delta) = y_0 \sum_{j=0}^{\infty} \sum_{k=0}^j \frac{(-\mu)^{j-k} \lambda^k}{(j-k)!k!(1+\alpha)^k} \delta^{j+k\alpha} = y_0 \sum_{n=0}^{\infty} \frac{(-\mu\delta)^n}{n!} \sum_{k=0}^{\infty} \frac{1}{k!} \left(\frac{\lambda\delta^{1+\alpha}}{1+\alpha} \right)^k = y_0 \exp\left(-\mu\delta + \lambda \frac{\delta^{1+\alpha}}{1+\alpha}\right),$$

which is the expected solution at $t = \delta$ to $\partial_t y = (-\mu + \lambda(\delta - t)^\alpha)y$, $y(t_0) = y_0$, in the standard diffusion in time case.

Therefore, the application of Theorems 1 to 4, together with (16), allows us to derive the following two results.

Corollary 3 (Full fractional Stejskal–Tanner formula, $\mu = 0$). *The Stejskal–Tanner formula for the acquired signal at the bore (centreline) of the magnetic field in the full time-space fractional Bloch–Torrey setting (12) is*

$$S/S_0 = \sum_{j=0}^{\infty} \theta_j \left(\lambda \delta^{\alpha+\beta} \right)^j E_\beta \left(\lambda \delta^\alpha (\Delta - \delta)^\beta \right) \sum_{j=0}^{\infty} \xi_j \left(\lambda \delta^{\alpha+\beta} \right)^j, \quad (25)$$

where $\lambda = -\tau_\beta^{1-\beta} \tau_\alpha^{\alpha/2-1} (\mathbf{g}^T \mathbf{D} \mathbf{g})^{\alpha/2} (\gamma G)^\alpha$, and coefficients θ_j and ξ_j are given by equations (17b) and (22b).

For $\beta = 1$, and following the particularisation of results presented in Theorems 1 and 3, the expression above reduces to

$$S/S_0 = \exp\left(\lambda \frac{\delta^{1+\alpha}}{1+\alpha}\right) \exp\left(\lambda \delta^\alpha (\Delta - \delta)\right) \exp\left(\lambda \frac{\delta^{1+\alpha}}{1+\alpha}\right) = \exp\left(\lambda \delta^\alpha \left(\Delta - \delta \frac{\alpha-1}{\alpha+1}\right)\right),$$

which with $\lambda = -\tau_\alpha^{\alpha/2-1} (\mathbf{g}^T \mathbf{D} \mathbf{g})^{\alpha/2} (\gamma G)^\alpha$ recovers the results of (11) for the space-fractional Bloch–Torrey equation.

Corollary 4 (Full fractional Stejskal–Tanner formula, $\mu \neq 0$). *The Stejskal–Tanner formula for the acquired signal in the full time-space fractional Bloch–Torrey setting (12) is*

$$S/S_0 = \left(\sum_{j=0}^{\infty} \sum_{k=0}^j \mu^{j-k} \lambda^k \theta_{j,k} \delta^{j\beta+k\alpha} \right) E_\beta \left(\lambda \delta^\alpha (\Delta - \delta)^\beta \right) \left(\sum_{j=0}^{\infty} \sum_{k=0}^j (-\mu)^{j-k} \lambda^k \xi_{j,k} \delta^{j\beta+k\alpha} \right), \quad (26)$$

where $\mu = -\tau_\beta^{1-\beta} i\gamma G \mathbf{r} \cdot \mathbf{g}$, $\lambda = -\tau_\beta^{1-\beta} \tau_\alpha^{\alpha/2-1} (\mathbf{g}^T \mathbf{D} \mathbf{g})^{\alpha/2} (\gamma G)^\alpha$, and coefficients $\theta_{j,k}$ and $\xi_{j,k}$ are given by equations (18b) and (24b).

For $\beta = 1$, and following the particularisation of results presented in Theorems 2 and 4, the expression above reduces to

$$S/S_0 = \exp\left(\mu\delta + \lambda \frac{\delta^{1+\alpha}}{1+\alpha}\right) \exp\left(\lambda \delta^\alpha (\Delta - \delta)\right) \exp\left(-\mu\delta + \lambda \frac{\delta^{1+\alpha}}{1+\alpha}\right) = \exp\left(\lambda \delta^\alpha \left(\Delta - \delta \frac{\alpha-1}{\alpha+1}\right)\right),$$

which with $\lambda = -\tau_\alpha^{\alpha/2-1} (\mathbf{g}^T \mathbf{D} \mathbf{g})^{\alpha/2} (\gamma G)^\alpha$ newly recovers the results of (11) for the space-fractional case.

4. Results

4.1. Acquired signal decays at the bore of the magnetic field ($\mu = 0$)

The acquired signal decay at bore of the magnetic field ($\mu = 0$) in the full time-space fractional Bloch–Torrey setting, as provided by (25), is given by the multiplication of the two series associated with the positive and negative pulses of the Stejskal–Tanner sequence, and the one-parametric Mittag–Leffler function associated with the interval between pulses. Whereas the convergence of the classical Mittag–Leffler function is well established and efficient algorithms exist for its computation (as used here on its numerical evaluation, in the form of integrals in the complex plane of its Laplace transform [23]), we first address the convergence of the two other parts of the solution. As

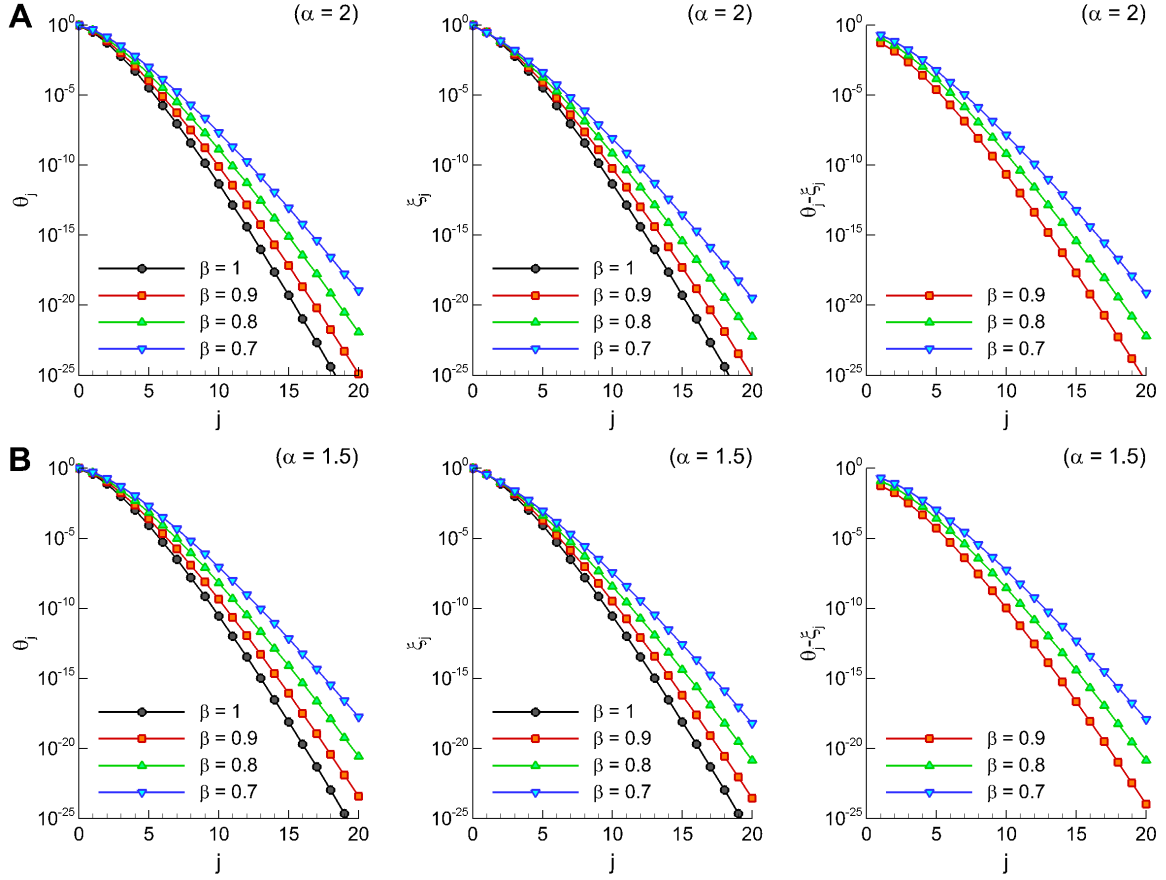


Figure 3: Convergence of the series associated with the encoding pulses of the Stejskal-Tanner sequence in the fractional Bloch-Torrey equation at the bore of the magnetic field ($\mu = 0$). **A:** For $\alpha = 2$ and varying fractional derivative order β , coefficients θ_j associated to the positive pulse of the sequence (left panel), coefficients ξ_j associated to the negative pulse of the sequence (middle panel), and difference of coefficients to highlight the non-symmetry of the two parts of the solution in the time-fractional case (right panel, $\theta_j = \xi_j$ only for $\beta = 1$). **B:** Equivalent results in the presence of a space-fractional derivative component ($\alpha = 1.5$), with rate of convergence primarily determined by β .

established in [24, pp. 106-107] for the three-parametric (Kilbas-Saigo) Mittag-Leffler function through the use of the asymptotic formula when $z \rightarrow \infty$ for the quotient of Gamma functions

$$\frac{\Gamma(z+a)}{\Gamma(z+b)} \approx z^{a-b} \left[1 + \frac{(a-b)(a+b-1)}{2z} + \dots \right],$$

then as $j \rightarrow \infty$ coefficients θ_j and ξ_j satisfy

$$\frac{\theta_{j-1}}{\theta_j} = \frac{\Gamma(1+j(\alpha+\beta))}{\Gamma(1+j(\alpha+\beta)-\beta)} \approx [j(\alpha+\beta)]^\beta \rightarrow \infty, \quad (27a)$$

$$\frac{\xi_{j-1}}{\xi_j} = \frac{\Gamma(1+j(\alpha+\beta))}{\Gamma(1+j(\alpha+\beta)-(\alpha+\beta))} \frac{\Gamma(j(\alpha+\beta)-\alpha)}{\Gamma(j(\alpha+\beta))} \approx [j(\alpha+\beta)]^{\alpha+\beta} [j(\alpha+\beta)]^{-\alpha} = [j(\alpha+\beta)]^\beta \rightarrow \infty, \quad (27b)$$

and therefore the radius of convergence of both series is equal to $+\infty$. Furthermore, the two series exhibit the same convergence rate, which is primarily determined by its fractional power in β . This is further illustrated in Figure 3 for $\alpha = 2$ (Fig. 3A) and $\alpha = 1.5$ (Fig. 3B), where small variations in the time-fractional derivative order β exhibit more pronounced reductions in convergence rate compared to larger variations in the space-fractional order α , for both

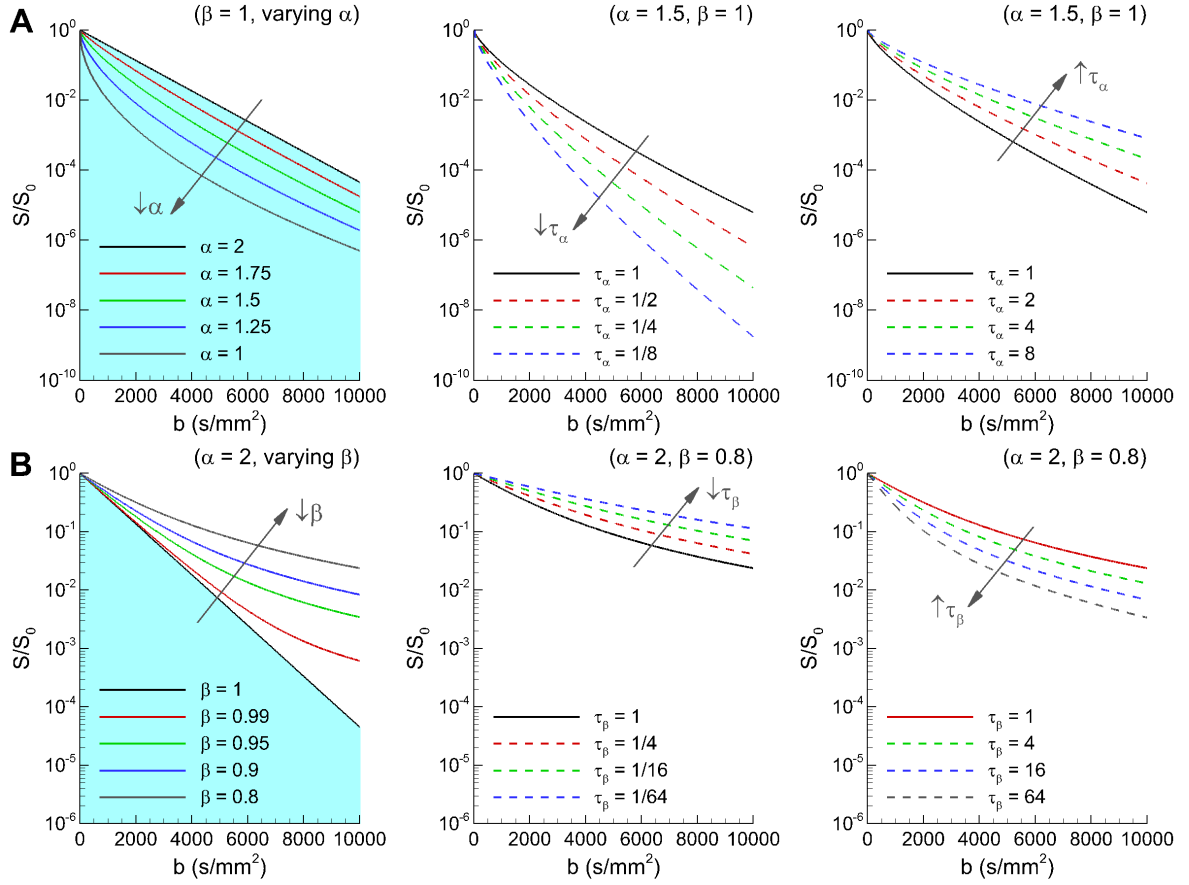


Figure 4: Signal decay in the full fractional Bloch–Torrey equation at the bore of the magnetic field ($\mu = 0$). **A:** For $\beta = 1$, a space-fractional derivative component ($1 < \alpha < 2$) yields a super-diffusive anomalous decay of the solutions (left panel, shaded regions of the plots). Decreasing or increasing the space-fractional scaling factor τ_α results in the accentuation (middle panel) or attenuation (right panel) of the super-diffusive decay, respectively. **B:** A reverse behaviour is observed under a time-fractional derivative component ($0 < \beta < 1$) for $\alpha = 2$, with solutions exhibiting incursions into the sub-diffusive regime (left panel, non-shaded regions of the plots). Decreasing or increasing the time-fractional scaling factor τ_β results in the accentuation (middle panel) or attenuation (right panel) of the sub-diffusive decay, respectively. In all plots, the range of b values was generated by varying the magnitude of the applied gradient in the Stejskal–Tanner sequence, with $\Delta = 20$ ms, $\delta = 3$ ms, and considering an isotropic diffusion tensor with $D = 10^{-3}$ mm²/s. Unspecified parameters are set to unit values.

coefficients θ_j and ξ_j (Fig. 3, left and middle columns, respectively). Moreover, in spite of the same convergence rate and similar magnitudes, the difference of coefficients $\theta_j - \xi_j$ (Fig. 3, right column) highlights the non-symmetry of these two parts of the solution in the time-fractional case. This implies that, for all $0 < \beta < 1$, the positive and negative pulses cannot be assumed as having the same contribution to the total acquired signal decay as in the standard diffusion case, reflecting non-identical random walks during the positive and negative pulse gradients of the sequence [25, 26].

For the evaluation of signal decays, we mimic experimental protocols in investigations of anomalous diffusion, by generating a broad range of b values associated to varying the magnitude of the applied gradient G in the Stejskal–Tanner sequence. The magnitude of the applied gradient G is unambiguously obtained through the established relationship $b = (\gamma G \delta)^2 (\Delta - \delta/3)$, and used in the numerical evaluation of signal decays for varying α and β . Equivalently, results are presented against their associated b values, as routinely performed in experimental and clinical practice.

Following this approach, signal decays at the bore of the magnetic field are shown in Figure 4, with $\Delta = 20$ ms, $\delta = 3$ ms [4]. For additional clarity, signal decays were evaluated considering an isotropic diffusion tensor, using $D = 10^{-3}$ mm²/s for water diffusion, and all series computed up to an absolute precision of $\varepsilon = 10^{-14}$. For the types of fractional derivatives considered, the mean square displacement of the density distributions associated to the Bloch–

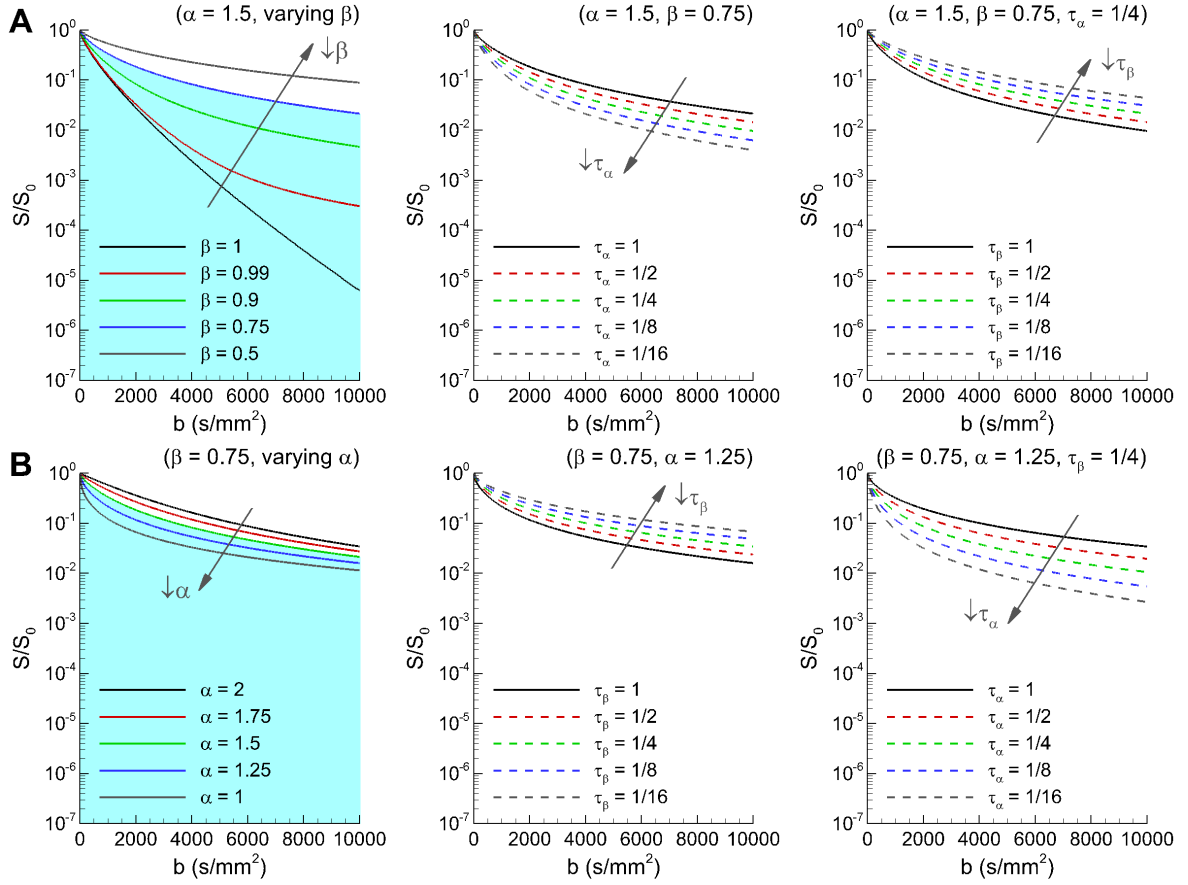


Figure 5: Signal decay in the full fractional Bloch–Torrey equation at the bore of the magnetic field ($\mu = 0$), with mixed fractional derivative orders. **A:** A gradual decrease in β in the presence of a space-fractional derivative component ($\alpha = 1.5$, left panel) allows for a transition from a super-diffusive behaviour (given by $2\beta > \alpha$, shaded regions of the plot) into the sub-diffusive regime (given by $2\beta < \alpha$, non-shaded regions). Decreasing the space-fractional (τ_α) or time-fractional (τ_β) scaling factors results in the accentuation of their respective anomalous behaviours (middle and right columns, respectively). **B:** Equivalently, a gradual decrease in α in the presence of a time-derivative fractional component ($\beta = 0.75$, left panel) deviates the signal decay into the super-diffusive regime ($2\beta > \alpha$, shaded regions of the plot), although with a smaller effect on signal amplitude at large b values. Role of the time-fractional or space-fractional scaling factors (middle and right columns, respectively) as described in A. Sequence parameters: $\Delta = 20$ ms, $\delta = 3$ ms, considering an isotropic diffusion tensor with $D = 10^{-3}$ mm²/s. Unspecified parameters are set to unit values.

Torrey equation is well established as $\langle x^2 \rangle \propto t^{2\beta/\alpha}$ [27], and hence $2\beta > \alpha$ and $2\beta < \alpha$ respectively represent the regions of super-diffusive and sub-diffusive behaviour of the solutions. Therefore, for $\beta = 1$, a space-fractional derivative component ($1 < \alpha < 2$) always yields a super-diffusive anomalous decay (Fig. 4A, left panel, shaded regions of the plots), whereas for $\alpha = 2$ solutions under a time-fractional derivative component ($0 < \beta < 1$) exhibit incursions into the sub-diffusive regime (Fig. 4B, left panel, non-shaded regions of the plots). For both fractional derivative orders, decreasing the scaling factors τ_α and τ_β below unity results in the accentuation of the respective super-diffusive or sub-diffusive behaviours (Fig. 4, middle column). Conversely, large values of τ_α or τ_β above unity result in signal decays transitioning from the super-diffusive into the sub-diffusive regimes (Fig. 4, right column). For uniqueness in model response with respect to each fractional derivative type, this hence implies the use of scaling factors in the bounded interval $0 < \tau_\alpha, \tau_\beta \leq 1$ in order to ensure the desired separation of phenomena. The need of such a separation can be further explored in future studies by analysis of appropriate experimental data.

The effects of mixed fractional derivative orders on signal decay are presented in Figure 5. A gradual decrease in β in the presence of a space-fractional derivative component (Fig. 5A, left column) allows for a transition from the original super-diffusive behaviour (as given by $2\beta > \alpha$, shaded regions of the plot) into the sub-diffusive regime

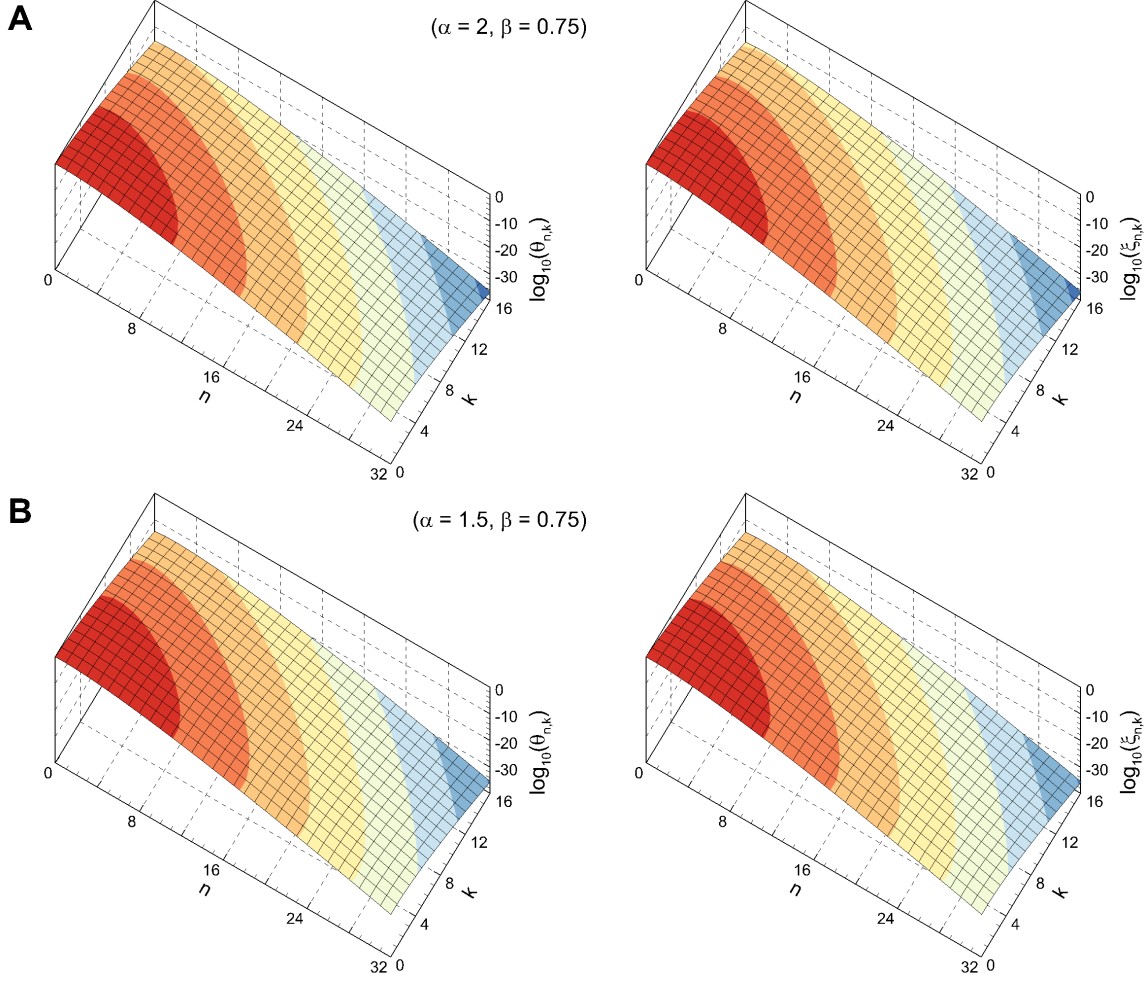


Figure 6: Coefficients of the double series associated with the positive ($\theta_{n,k}$, left panel) and negative ($\xi_{n,k}$, right panel) encoding pulses of the Stejskal–Tanner sequence in the fractional Bloch–Torrey equation outside the bore of the magnetic field ($\mu \neq 0$). In these plots, n indicates the diagonal number in the structure of the solutions shown in Fig. 2. Results are presented for both sub-diffusive (panel A; $\alpha = 2, \beta = 0.75$; $2\beta < \alpha$) and pseudo-Gaussian (panel B; $\alpha = 1.5, \beta = 0.75$; $2\beta = \alpha$) regimes, exhibiting similar orders of convergence in both cases.

($2\beta < \alpha$, non-shaded regions). Equivalently, a gradual decrease in α in the presence of a time-fractional derivative component (Fig. 5B, left column) deviates the signal decay into the super-diffusive regime ($2\beta > \alpha$, shaded regions of the plot). However, these results illustrate a stronger role of the time fractional derivative in modulating signal amplitude at large b values than its space fractional counterpart. The fractional scaling factors hold the same effects as described above, accentuating the super-diffusive or sub-diffusive behaviours as $\tau_\alpha \rightarrow 0$ or $\tau_\beta \rightarrow 0$, respectively (Fig. 5, middle and right columns).

4.2. Acquired signal decays outside the bore of the magnetic field ($\mu \neq 0$)

Figure 6 illustrates the coefficients of the two double series associated in (26) with the positive and negative pulses of the Stejskal–Tanner sequence outside the bore of the magnetic field ($\mu \neq 0$). The coefficients are presented in the form $\theta_{n,k}$, where n indicates the diagonal number in the structure of the solutions shown in Fig. 2. This allows for a

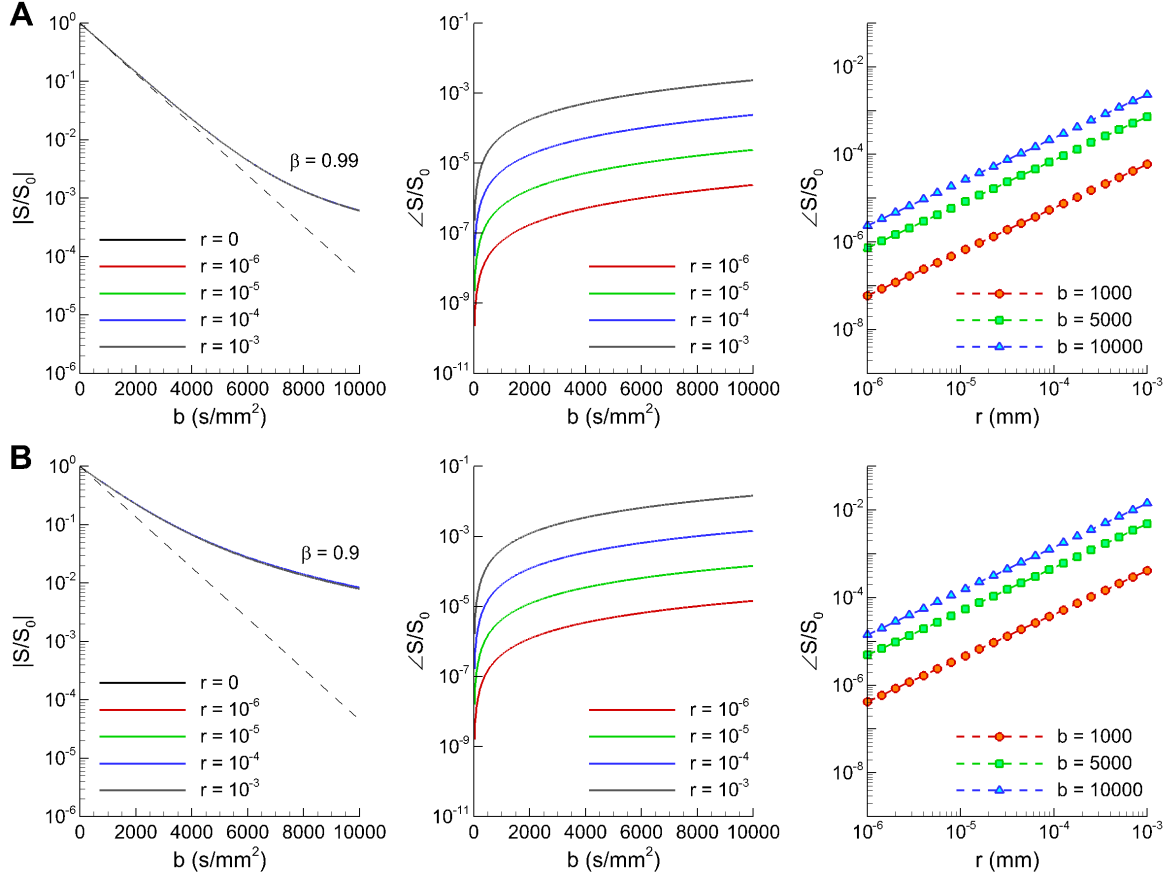


Figure 7: Signal decay in the full fractional Bloch–Torrey equation outside the bore of the magnetic field ($\mu \neq 0$). **A:** Amplitude of acquired signal decays as a function of the distance to the bore (left panel) for $\alpha = 2$ and $\beta = 0.99$, and resulting phase shifts in the acquired signals as a function of the amplitude of the encoding gradient (middle panel) and distance to the bore (right panel). **B:** Same as A, but for a larger decrease of the time-fractional component from unity ($\beta = 0.9$). Sequence parameters: $\Delta = 20$ ms, $\delta = 3$ ms, considering an isotropic diffusion tensor with $D = 10^{-3}$ mm²/s. The dashed lines in the left panels indicate the standard diffusion signal decay. Unspecified parameters are set to unit values.

more straightforward evaluation of each double series as

$$\sum_{j=0}^{\infty} \sum_{k=0}^j \mu^{j-k} \lambda^k \theta_{j,k} \delta^{j\beta+k\alpha} = \sum_{n=0}^{\infty} (\mu \delta^{\beta})^n \sum_{k=0}^{\infty} \theta_{n+k,k} (\lambda \delta^{\alpha+\beta})^k,$$

and equivalently for the series in $\xi_{j,k}$. Coefficients $\theta_{n,k}$ and $\xi_{n,k}$ exhibit convergence rates analogous to those of coefficients θ_j and ξ_j in (27a)–(27b) (which correspond to $n = 0$ in Fig. 6). However, a shortcoming of the obtained analytical solutions to the fractional Bloch–Torrey equation is their form as a series expansion in positive powers of $\mu \delta^{\beta}$ and $\lambda \delta^{\alpha+\beta}$. At $b = 10000$ s/mm², for our choice of sequence parameters and at a distance as small as 0.05 mm in the direction of the encoding pulse, even for standard diffusion this implies that $\lambda \delta^{\alpha+\beta} = -1.5789$, whereas $\mu \delta^{\beta} = -36.2738i$. The direct evaluation of powers in $\mu \delta^{\beta}$ hence quickly results into double-precision overflows in spite of the $+\infty$ radius of convergence of the series. The same difficulties hold if the series is evaluated either in row or column order. A possible approach to circumvent these limitations when $\Delta \gg \delta$ is the use of the so-called narrow pulse approximation, which simplifies the description for the gradient pulses by using Dirac delta functions, hence reducing the contribution to signal decay to that of the central interval of the encoding sequence. In the case of standard diffusion ($\alpha = 2, \beta = 1$), this simplifies (6) to $S/S_0 \approx \exp\left(-(\gamma G \delta)^2 \Delta \mathbf{g}^T \mathbf{D} \mathbf{g}\right)$. For the full time-space fractional Bloch–Torrey setting given by

(26), this translates into

$$S/S_0 \approx E_\beta \left(-\tau_\beta^{1-\beta} \tau_\alpha^{\alpha/2-1} (\gamma G \delta)^\alpha \Delta^\beta (\mathbf{g}^T \mathbf{D} \mathbf{g})^{\alpha/2} \right).$$

Nevertheless, such an approximation eliminates the spatial dependence of the solutions, encoded in μ by the $\mathbf{r} \cdot \mathbf{g}$ term.

Given these constraints, we therefore restrict the evaluation of (26) without the narrow pulse approximation to distances up to $\mathbf{r} \cdot \mathbf{g} = 10^{-3}$ mm (note that \mathbf{r} has units of space, whereas \mathbf{g} is a dimensionless unit direction vector), which avoided the above described double-precision overflows for all considered values of α and β . For the range of distances considered, the presence of a fractional time derivative component does not induce substantial differences in the amplitude of the acquired signal decays compared to those at the bore of the magnetic field (Fig. 7, left column). However, and even for $\beta \approx 1$, the time-fractional Bloch–Torrey model predicts a residual shift in phase of the acquired signals as a function of the magnitude of the encoding gradient (Fig. 7, middle column) and the distance to the bore (Fig. 7, right column). This results as a consequence of the no net cancellation of the imaginary parts arising from the positive and negative gradient pulses, which only counteract for $\beta = 1$ given their multiplication in the form of exponentials. The asymptotic decay of phase shifts at $b = 0$ to $-\infty$ in logarithmic scale also indicates zero phase acquisition in the absence of applied magnetic field. Importantly, such a residual phase shift is in physical agreement with the phase acquisition experienced by water protons undergoing diffusion [25], [26, pp. 204–210]. In their motion, the spins experience differing phase shifts due to non-identical random walks during the positive and negative gradients of the encoding sequence. This is another characteristic of magnetic resonance imaging in biological tissues and structural heterogeneous media, not predicted by the standard diffusion Bloch–Torrey model.

5. Discussion

In this paper, we have derived the exact solution to the fractional time-space Bloch–Torrey equation for MRI, posed in terms of the space fractional Laplacian and the time fractional Caputo derivative. By exploiting the piecewise nature of the Stejskal–Tanner sequence, the problem is rewritten as three consecutive time-fractional equations of polynomial nature. Whereas the subproblem associated to the time between pulses has a straightforward solution as the one-parametric Mittag–Leffler function, those related to the positive and negative pulses of the sequence represent a much bigger challenge given their non-autonomous character. Their solutions are obtained around extended (Kilbas–Saigo) Mittag–Leffler and Lauricella functions of the second kind. Regardless of the complexity of Lauricella functions, their evaluation as Gauss hypergeometric functions further allows us to derive compact Stejskal–Tanner formulas for the acquired signal decay at the end of the sequence. The numerical evaluation of the obtained formulas demonstrates that our solutions replicate the super-diffusive and sub-diffusive regimes reported in MRI studies. These have been previously shown to arise from local magnetisation gradients between compartments with different magnetic susceptibility, capillary perfusion, porous media or stationary random flows, intravoxel incoherent motion, and hindered transport in densely packed and heterogeneous structures [14]. Moreover, our solutions at the end of the sequence exhibit residual phase shifts as those associated with the microscopic motion (i.e. diffusion) of water protons in MRI, due to non-identical random walks during the positive and negative pulse gradients [25, 26]. None of these characteristics of MRI in biological tissues and structurally-complex materials are replicated by the Bloch–Torrey model under the assumptions of standard diffusion ($\alpha = 2, \beta = 1$).

Compared with existing literature on exact solutions to the fractional Bloch–Torrey equation, our results for the space-fractional Laplacian are analogous to those previously derived considering sequential Riesz fractional operators in space [28–30]. On the contrary, analytical solutions to the time-fractional setting have only been presented in the absence of diffusion [31], under the simplest case of an applied constant magnetic gradient and with no-crossed terms [7], or for modified versions of the Bloch–Torrey equation [8, 32]. Even in the latter case, Stejskal–Tanner formulas for the acquired signals were not presented given their complexity. Our findings therefore augment these previous results by considering the non-modified full fractional time-space Bloch–Torrey equation, including appropriate fractional scaling factors to ensure the consistency of units. Extension of our results to more complex spin echo pulse sequences [29] can be easily obtained by still exploiting their piecewise nature, and concatenating additional terms associated to the positive and negative pulse gradients in the Stejskal–Tanner formulas as derived in this contribution. Our framework is also extensible to other fractional derivative types, for example time-fractional Riemann–Liouville operators given their close relationships with Caputo derivatives.

Our results also constitute a relevant contribution to the analysis of non-autonomous fractional differential equations of the form $\partial_t^\beta y = p(t)y$, where $p(t)$ is a polynomial of order α . Whilst the problem for $p(t) = \lambda t^\alpha$ has been previously addressed and solved as generalised (Kilbas–Saigo) Mittag–Leffler functions [20, 21], our solutions when $p(t) = \mu + \lambda t^\alpha$ represent an extension of the former in terms of an intricate convolution between these three-parametric and the classical one-parametric Mittag–Leffler functions. Moreover, we are not aware of any previous studies considering polynomials of the form $p(t) = -\mu + \lambda(\delta - t)^\alpha$, where the contribution of the polynomial term varies in the opposite direction to the time increase in the fractional differential operator. The solution to this problem is presented here around the above mentioned Lauricella functions of the second kind. There only exist a small number of references in the literature relating these functions to the solution of some Volterra-type fractional integro-differential equations [33, 34] and fractional kinetic equations [35], still of a different nature to the problem considered here. In addition, the coefficients $\theta_{j,k}$ and $\xi_{j,k}$ of the double series from the two pulses of the Stejskal–Tanner sequence are in close resemblance with those of the three-parametric Kilbas–Saigo function. This suggests the possible existence of a more general class of Mittag–Leffler functions, which might encompass the contribution from both terms. Future extensions of the theoretical results presented here might also include considering time-fractional derivatives of order $\beta > 1$, which would expand the range of model dynamics to oscillatory relaxation processes [36].

Nevertheless, an important limitation of our space-time fractional Stejskal–Tanner formulas is their form as a series expansion in positive powers of $\mu\delta^\beta$ and $\lambda\delta^{\alpha+\beta}$. This severely constrains the range of distances from the centre of the bore (encoded in the model parameter μ) for which we were able to report numerical approximations to the acquired signal decay, due to double-precision overflows regardless of the infinity radius of convergence of the series. Such a challenge is not specific to our problem; for example, it also arises in the direct evaluation of the one-parametric Mittag–Leffler function (or even the exponential) using its series expansion for large values of the argument. However, efficient algorithms circumventing these shortcomings have been developed for the computation of other types of Mittag–Leffler functions [23]. An engagement of the community in developing the appropriate numerical tools for the accurate evaluation of these extended (Kilbas–Saigo) Mittag–Leffler functions might further increase the value of the results presented in this paper. One possibility in this regard might be the use of global Padé approximations, which have been proven useful in the accurate and efficient evaluation of other types of Mittag–Leffler functions [37, 38]. A related but different approach might involve using peridynamics models with fractional power law kernels in order to model the Bloch–Torrey equation. In this respect, the results presented in [39], where the Fourier coefficients of a non-local peridynamic continuum model were shown to converge to those of the original Laplace operator, may also help to improve convergence rates.

6. Conclusion

In this contribution, we have presented a new analytical framework for the solution of the fractional time-space Bloch–Torrey equation for magnetic resonance imaging. In particular, our analytical solutions widen the types of fractional order differential equations that can be directly solved, especially those associated with α -analytic solutions of non-autonomous fractional differential equations with variable coefficients [40]. Moreover, our results may have important implications in advancing our current interpretation of MRI, given the broad range of physical responses retrieved by the attained exact solutions to the fractional time-space Bloch–Torrey equation (super-diffusive and sub-diffusive regimes of anomalous signal decay, and incomplete refocusing of spins at the end of the encoding sequence). The application of our results in future studies to experimental data may yield a better MRI characterisation of tissue microstructure in both healthy and diseased states (analysis of orthotropic tissue such as tendons, ligaments, muscle fibres or white matter tracks), through the estimation of tissue properties based on exact solutions to the underlying diffusive processes, rather than the fitting of experimental data to phenomenological signal decays or solutions of *ad hoc* models. In addition, this may also yield an improved parameterisation of modelling and simulation fractional diffusion frameworks of different biological processes [41–45], which are gaining much attention in the field of the applied sciences to unravel the many facets of the modulation of biological function by tissue microstructure.

Acknowledgments

Alfonso Bueno-Orovio acknowledges the support from the National Centre for the Replacement, Refinement & Reduction of Animals in Research through an Infrastructure for Impact Award (NC/P001076/1), the British Heart

Foundation Centre for Research Excellence (RE/13/1/30181), and the CompBioMed Centre of Excellence in Computational Biomedicine (European Union grant agreement No. 675451). Kevin Burrage acknowledges the support from the Australian Research Council (ARC; www.arc.gov.au/), through its Centre of Excellence for Mathematical and Statistical Frontiers (ACEMS; CE140100049). The authors also thank the reviewers of this manuscript for their constructive and insightful comments, which have greatly contributed to improving its final version. The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript. The authors declare no conflict of interests.

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