Accepted to J. Chem. Phys. 10.1063/5.0148175

Nuclear Magnetic Resonance signal decay in presence of a background gradient: normal and anomalous diffusion

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(Dated: 12 April 2023)

A novel way for calculating the diffusion-weighted NMR attenuation signal expression in presence of a background gradient is developed. This method is easily applicable to NMR attenuated signals arising from any pulse field gradient (PFG) sequence experiments. Here we provide the detailed calculations for the classical pulsed gradient stimulated echo (PGSTE) and the pulsed gradient spin echo (PGSE), as particular case. Within this general theoretical framework, devised for Gaussian processes with stationary increments, we recover and extend the previous Stejskal-Tanner results in case of normal diffusion and furnish a new expression in case of anomalous diffusion.

I. INTRODUCTION

The NMR potential of spin-echo experiments in measuring the self-diffusion coefficient was firstly indicated by Hahn in his pioneering work of 1950[1]. After that, the pulse field gradient (PFG) method has become an entrenched non-invasive technique for the investigation of the molecular motion and dynamics.

The basic PFG sequence is the so-called pulse-gradient spin-echo (PGSE)[2–5], in which, after a radio-frequency (rf) 90° pulse, a short gradient pulse of amplitude $\mathbf{g}$ and duration δ confers phase shifts to the spins. A second equivalent gradient pulse, after an intermediate 180° rf-pulse, reverses the phase shifts to yield an attenuated signal decay, as a consequence of the molecular spins movement during the diffusion time Δ. The theory developed by Stejskal and Tanner in their celebrated paper[2], furnished the correct formula to analyze the NMR spin-echo attenuation signal, stemming from the Bloch-Torrey equation for the spin magnetization in the form introduced by Abragam[6]. The paper of Hahn[1] showed how the use of three 90° rf-pulses create an echo with an attenuation having a peculiar dependence on the spin-lattice relaxation time T_1. A such characteristic makes possible to abate the effect of the spin-spin relaxation T_2 on the signal and extend considerably the diffusion time Δ in the measurements as shown in the paper of Tanner[7]. Opposite to the spin-echo of PGSE experiment, in this case the measured echo was named by Hahn "stimulated-echo"[1], so that this kind of PFG sequence goes under the name of pulse-gradient stimulated-echo (PGSTE). The theory developed by Tanner to accomplish a final fitting formula for the PGSTE attenuation signals, was entirely based on the assumption that the spin stochastic trajectories are described by random walks.

Very importantly, in both PGSE and PGSTE theoretical analysis, the authors assume the presence of a generic time-dependent gradient and derive analytical results for the case with a constant imposed gradient $\mathbf{g}$ combined with a constant background gradient of magnitude $\mathbf{g}_0$. The contribution of uncontrollable internal gradients to NMR signal decay is a delicate and important issue in various contexts. Biological tissues[8–10], porous media[11,12], and in general, many heterogeneous structures exhibit microscopic variations in magnetic susceptibility, caused by imperfect shimming, heterogeneous magnetic susceptibility within the object, for example, near tissue-air interfaces or in meso- and microscopically heterogeneous tissue[13]. In all these cases, internal field gradients that are generated may be extraordinarily strong. Depending on their scale, these background gradients provide image distortion[14], increased rates of dephasing (reduced T_2-times)[15], unwanted diffusion-weighting[16] that can lead to a wrong interpretation of the diffusion phenomena[17]. Adopting a simple PGSE sequence in this type of systems alters the measure of the apparent diffusion coefficient, if $\mathbf{g}_0$ does not approaches zero, since the $\mathbf{g}_0^2$ and $\mathbf{g}\cdot\mathbf{g}_0$ terms cannot be neglected[2,16,18–20]. The same problem arises when a PGSTE sequence is applied, rather than a PGSE[21,22]. To overcome this issue, a large variety of PFG sequences has been optimized in order to mitigate the effect of such a background gradient and to obtain a more liable estimate of the molecules self-diffusion inside a sample[23–33]. A tentative attempt of grouping this wealth of PFG sequences can be made according to the notation introduced in[34]. Sequences where the spin echo NMR signal arises due to the phase inversion properties of 180° rf-pulses are called Alternating PFG experiments (APFG) based on Carr-Purcell-Meiboom-Gill (CPMG). For these sequences the Bloch-Torrey equation still applies and a formal solution, such that provided by Stejskall and Tanner for PGSE, holds[25]. On the other side, any sequence involving three 90° rf-pulses is named as APFG based on the stimulated spin echo (STE). Unfortunately, the Tanner's PGSTE formal solution[7] is not easily extended to encompass more general situations, and no analytical alternative derivation is provided on the other side. Indeed, the starting point is the assumption of the validity of the Torrey solution of the Bloch-Torrey equation, although with a time dependent gradient $\mathbf{g}$[34]. Among these, some studies report the more realistic situation where the background gradient $\mathbf{g}_0$ is not constant, exhibiting an explicit time dependence[31,32]. In these works, however, although on one hand the PFG sequences are such that the influence of the background gradient is canceled out, on the other the decay signal is significantly reduced, resulting in a lower sensitivity in the diffusion measurements.

In Ref.[35] we provided a general theoretical framework for the correct interpretation of NMR attenuation signals coming from PGSE experiments, in the case of Gaussian systems with stationary increments. In these systems the molecular propagator is assumed to have a Gaussian shape at any time, and the velocity as well as the position correlation function, $\langle v(t_1)v(t_2)\rangle$ or $\langle x(t_1)x(t_2)\rangle$ respectively, depends simply on $|t_1-t_2|$. These are the underlying assumptions for many physical processes, among which, but not only, those satisfying the Bloch-Torrey equation.

We hereby extend the scheme furnished in Ref.[35], providing an unifying exact theoretical framework that encompasses any kind of PFG experiment, be APFG CPMG-like or STE-like, in presence of a constant background gradient. We focus our analysis on the simplest cases, furnishing the detailed calculations for PGSE and PGSTE sequences, stressing the fact that these could be extended to any other PFG sequence, without any need to resort to the Bloch-Torrey equation or to specific ansatz. On top of that, our theoretical approach broadens the PGSE and PGSTE classical expressions to the case of normal-diffusing systems with general viscous drag.

Most importantly, the universal nature of our framework goes beyond its formal validity comprehensive of the entire class of PFG experiments. Indeed, the expressions encompassing the presence of a background gradient extend to NMR attenuation signals arising from systems displaying anomalous diffusion and satisfying the hypothesis of Gaussianity and stationarity of the increments. For these systems, the molecular mean square displacement is characterized by a non-linear law of the type $\langle (x-\langle x\rangle)^2\rangle \sim t^{\alpha}$, with $\alpha \in (0,2]$, rather than the Brownian case usually treated in literature ($\langle (x-\langle x\rangle)^2\rangle \sim t$).

The paper is structured as follows. In Sec.II we recall the PGSTE sequence and show how it fits into our theoretical framework. We also develop the general symbolic calculation which allows deriving the final fitting formula for NMR attenuation signals from PGSTE experiments. In Sec.III we specify the fitting formula to the case of normal diffusion, while in Sec.IV we extend it to the case of anomalous diffusion. In Sec.V we present some concluding remarks.

II. NMR SIGNAL DECAY IN PRESENCE OF A BACKGROUND GRADIENT

Here we derive the diffusional attenuation of the nuclear magnetization in the plane perpendicular to the applied magnetic field $\mathbf{B}$, as a function of the rf-pulse times and of a variable field gradient $\mathbf{G}(t)$. In particular, we consider a system with a steady background gradient $\mathbf{g}_0$, and a second gradient $\mathbf{g}$, with a direction different than $\mathbf{g}_0$, which is turned on following a typical PGSTE sequence. The total gradient $\mathbf{G}$ that contributes to the diffusion in a PGSTE experiment is

$$\mathbf{G}(t) = \begin{cases} \mathbf{g}_0 & 0 \le t \le t_1 \\ \mathbf{g}_0+\mathbf{g} & t_1 \le t \le t_1+\delta \\ \mathbf{g}_0 & t_1+\delta \le t \le \tau_1 \\ 0 & \tau_1 \le t \le \tau_2 \\ -\mathbf{g}_0 & \tau_2 \le t \le t_1+\Delta \\ -\mathbf{g}_0-\mathbf{g} & t_1+\Delta\, t \le t_1+\Delta+\delta \\ -\mathbf{g}_0 & t_1+\Delta+\delta \le t \le t_e. \end{cases} \tag{1}$$

where t_1 and $t_1+\Delta$ are the times when the gradient $\mathbf{g}$ is turned on, δ is the duration of this gradient and τ_1 and τ_2 are defined in Fig.1.

The behavior during the time interval $\tau_1 \le t \le \tau_2$ is because in a classical PGSTE experiment the spin angle phases are stored in the z direction and they are unaffected by the field gradient.

The transverse magnetization of a spin-bearing particle (or molecule) can be expressed via the phase built up during the motion in a magnetic field gradient. The NMR signal attenuation is defined as the ensemble average spin echo amplitude, properly normalized[36]:

$$\frac{S(t_e)}{S(0)} = \langle e^{i\gamma\int_0^{t_e} dt\,\mathbf{v}(t)\cdot\mathbf{F}(t)}\rangle, \tag{2}$$

where $S(0)$ is the initial value of the signal, γ is the gyromagnetic ratio and $\mathbf{v}(t)$ represents the stochastic velocity of the particle/molecule.

The term $\mathbf{F}(t)$ is the quantity $\int_0^t \mathbf{G}(t')dt'$ corresponding to the integral of the pulse gradient field. For the gradient in Eq.1 the explicit expression for $\mathbf{F}(t)$ is

$$\mathbf{F}(t) = \begin{cases} \mathbf{g}_0 t & 0 \le t \le t_1 \\ \mathbf{g}_0 t+\mathbf{g}(t-t_1) & t_1 \le t \le t_1+\delta \\ \mathbf{g}_0 t+\mathbf{g}\delta & t_1+\delta \le t \le \tau_1 \\ \mathbf{g}_0\tau_1+\mathbf{g}\delta & \tau_1 \le t \le \tau_2 \\ -\mathbf{g}_0(t-\tau_1-\tau_2)+\mathbf{g}\delta & \tau_2 \le t \le t_1+\Delta \\ -\mathbf{g}_0(t-\tau_1-\tau_2)-\mathbf{g}(t-t_1-\Delta-\delta) & t_1+\Delta \le t \le t_1+\Delta+\delta \\ -\mathbf{g}_0(t-\tau_1-\tau_2) & t_1+\Delta+\delta \le t \le t_e \end{cases} \tag{3}$$

Assuming an isotropic diffusion we can express the former equation as

$$\frac{S(t_e)}{S(0)} = \langle e^{i\gamma \int_0^{t_e} dt v_x(t) F_x(t)} \rangle \langle e^{i\gamma \int_0^{t_e} dt v_y(t) F_y(t)} \rangle \langle e^{i\gamma \int_0^{t_e} dt v_z(t) F_z(t)} \rangle. \quad (4)$$

Under the hypothesis of Gaussianity, the former expression can be expanded into cumulant to the second order, the so-called Gaussian approximation in cumulant expansion[37–44]:

$$\ln \frac{S(t_e)}{S(0)} \simeq -\gamma^2 \int_0^{t_e} dt_1 \int_0^{t_e} dt_2 \, C(t_1,t_2) \mathbf{F}(t_1) \cdot \mathbf{F}(t_2), \quad (5)$$

where $C(t_1,t_2)$ represents the stationary velocity autocorrelation function of one of the velocity components:

$$C(t_1,t_2) = \langle v_x(t_1) v_x(t_2) \rangle = \langle v_y(t_1) v_y(t_2) \rangle = \langle v_z(t_1) v_z(t_2) \rangle. \quad (6)$$

The assumption of stationarity instead assures that the correlation function $C(t_1,t_2) \propto |t_1 - t_2|$. Under these hypothesis, the NMR attenuation signal becomes[35]

$$\ln \frac{S(t_e)}{S(0)} \simeq -\gamma^2 \int_0^{t_e} C(s) ds \int_s^{t_e} \mathbf{F}(t) \cdot \mathbf{F}(t-s) \, dt. \quad (7)$$

At first, our analysis will focus on the quantity

$$F_c(s) = \int_s^{t_e} \mathbf{F}(t) \cdot \mathbf{F}(t-s) dt, \quad (8)$$

where, in analogy to Eq.(3), we introduce the time-shifted function

$$\mathbf{F}(t-s) = \begin{cases} \mathbf{g}_0(t-s) & s \le t \le t_1 + s \\ \mathbf{g}_0(t-s)t + \mathbf{g}(t-t_1) & t_1 + s \le t \le t_1 + s + \delta \\ \mathbf{g}_0(t-s) + \mathbf{g}\delta & t_1 + s + \delta \le t \le \tau_1 + s \\ \mathbf{g}_0 \tau_1 + \mathbf{g}\delta & \tau_1 + s \le t \le \tau_2 + s \\ -\mathbf{g}_0(t-s-\tau_1-\tau_2) + \mathbf{g}\delta & \tau_2 + s \le t \le t_1 + s + \Delta \\ -\mathbf{g}_0(t-s-\tau_1-\tau_2) - \mathbf{g}(t-s-t_1-\Delta-\delta) & t_1 + s + \Delta \le t \le t_1 + s + \Delta + \delta \\ -\mathbf{g}_0(t-s-\tau_1-\tau_2) & t_1 + s + \Delta + \delta \le t \le t_e + s \end{cases} \quad (9)$$

For the sake of clarity and to simplify the calculation of the quantity $F_c(s)$, we will adopt in the following a symbolic notation.

A. Symbolic calculation

From Eq.(3), given the piecewise nature of $\mathbf{F}(t)$, it is useful to consider the set of the interval extremes $\mathscr{A} = \{0, t_1, t_1 + \delta, \tau_1, \tau_2, t_1 + \Delta, t_1 + \Delta + \delta, t_e\} \equiv \{a_0, a_1, \cdots, a_7\}$. Equivalently, in view of Eq.(3) we can express the function $\mathbf{F}(t)$ in a symbolic compact form as

$$\mathbf{F}(t) = \begin{cases} \mathbf{F}_{i-1}(t) & a_{i-1} \le t \le a_i \\ 0 & t \ge a_7, \end{cases} \quad (10)$$

for $i \in [1,7]$.

In a similar way we define the set $\mathscr{B}(s) \equiv \{b_0(s), b_1(s), \cdots, b_7(s)\}$, with $b_i = a_i + s$, in reference of the domain of the shifted function $\mathbf{F}(t-s)$ in Eq.(9). Therefore, the function in Eq.(9) can be expressed as

$$\mathbf{F}(t-s) = \begin{cases} 0 & 0 \le t \le b_0(s) \\ \tilde{\mathbf{F}}_{i-1}(t-s) & b_{i-1}(s) \le t \le b_i(s) \end{cases} \quad (11)$$

where $b_i(s) = a_i + s$.

Let us refer to the Fig.2. Given a set $\mathscr{A}$, there will be values s and i satisfying the condition $b_{i-1}(s) = a_i$. However, we are interested in the minimum among these values, i.e.

$$s^{(1)}_{i,i-1} = \min_{i \in [1,7]} [a_i - a_{i-1}]. \quad (12)$$

Therefore, for any $s \le s^{(1)}_{i,i-1}$, the quantity in (8) is

Accepted to J. Chem. Phys. 10.1063/5.0148175

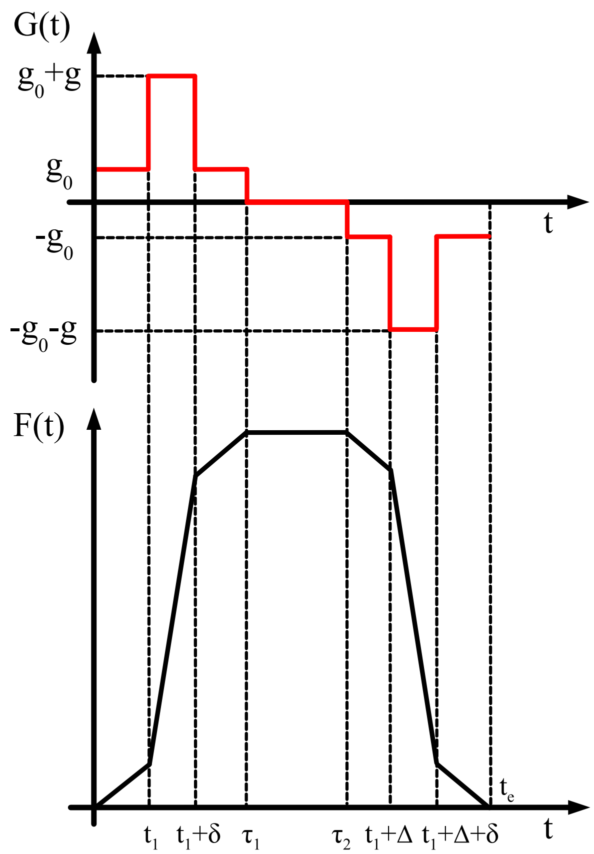

FIG. 1. Schematic representation of a single component of the gradient $\mathbf{G}(t)$ in Eq.(1) (top) and of $\mathbf{F}(t)$ in Eq.(3) (bottom).

$$
\begin{aligned}
F_c(s) \equiv A_0(s) = & \int_{b_0(s)}^{a_1} \mathbf{F}_0(t)\cdot\tilde{\mathbf{F}}_0 dt + \\
& \int_{a_1}^{b_1(s)} \mathbf{F}_1(t)\cdot\tilde{\mathbf{F}}_0(t-s)dt + \int_{b_1(s)}^{a_2} \mathbf{F}_1(t)\cdot\tilde{\mathbf{F}}_1(t-s)dt + \\
& \int_{a_2}^{b_2(s)} \mathbf{F}_2(t)\cdot\tilde{\mathbf{F}}_1(t-s)dt + \int_{b_2(s)}^{a_3} \mathbf{F}_2(t)\cdot\tilde{\mathbf{F}}_2(t-s)dt + \\
& \int_{a_3}^{b_3(s)} \mathbf{F}_3(t)\cdot\tilde{\mathbf{F}}_2(t-s)dt + \int_{b_3(s)}^{a_4} \mathbf{F}_3(t)\cdot\tilde{\mathbf{F}}_3(t-s)dt + \\
& \int_{a_4}^{b_4(s)} \mathbf{F}_4(t)\cdot\tilde{\mathbf{F}}_3(t-s)dt + \int_{b_4(s)}^{a_5} \mathbf{F}_4(t)\cdot\tilde{\mathbf{F}}_4(t-s)dt + \\
& \int_{a_5}^{b_5(s)} \mathbf{F}_5(t)\cdot\tilde{\mathbf{F}}_4(t-s)dt + \int_{b_5(s)}^{a_6} \mathbf{F}_5(t)\cdot\tilde{\mathbf{F}}_5(t-s)dt + \\
& \int_{a_6}^{b_6(s)} \mathbf{F}_6(t)\cdot\tilde{\mathbf{F}}_5(t-s)dt + \int_{b_6(s)}^{a_7} \mathbf{F}_6(t)\cdot\tilde{\mathbf{F}}_6(t-s)dt.
\end{aligned} \tag{13}
$$

For $s \geq s_{i,i-1}^{(1)}$, the expression of $F_c(s)$ in Eq.(13) does not hold anymore and ought to be changed. However, not any integral appearing in the sum (13) is modified. Indeed, it is easy to see that the integrals which must be modified are those having a_i and/or $b_{i-1}(s)$ as extremes of integration. Three cases can arise: $i=1$, $i=7$, $i \in [2,6]$

- $i=1$.

  We can express the change as

$$
\int_{b_0(s)}^{a_1} \mathbf{F}_0(t)\cdot\tilde{\mathbf{F}}_0(t-s)dt + \int_{a_1}^{b_1(s)} \mathbf{F}_1(t)\tilde{\mathbf{F}}_0(t-s)dt \tag{14}
$$

$$\Downarrow$$

$$
\int_{b_0(s)}^{b_1(s)} \mathbf{F}_1(t)\cdot\tilde{\mathbf{F}}_0(t-s)dt. \tag{15}
$$

  By subtracting the Eq.(14) from Eq.(15), we introduce the function $B_{1,0}^{(1)}(s)$ defined by

$$
\begin{aligned}
B_{1,0}^{(1)}(s) = & \int_{a_1}^{b_0(s)} \mathbf{F}_0(t)\cdot\tilde{\mathbf{F}}_0(t-s)dt + \\
& \int_{b_0(s)}^{a_1} \mathbf{F}_1(t)\cdot\tilde{\mathbf{F}}_0(t-s)dt
\end{aligned} \tag{16}
$$

- $i=7$.

  In this case the change in (13) involves the last two integrals:

$$
\int_{a_6}^{b_6(s)} \mathbf{F}_6(t)\cdot\tilde{\mathbf{F}}_5(t-s)dt + \int_{b_6}^{a_7(s)} \mathbf{F}_6(t)\tilde{\mathbf{F}}_6(t-s)dt \tag{17}
$$

$$\Downarrow$$

$$
\int_{a_6}^{a_7} \mathbf{F}_6(t)\cdot\tilde{\mathbf{F}}_5(t-s)dt. \tag{18}
$$

  The difference between the two is expressed as

$$
B_{7,6}^{(1)}(s) = \int_{a_7}^{b_6(s)} \mathbf{F}_6(t)\cdot\tilde{\mathbf{F}}_6(t-s)dt. \tag{19}
$$

- $i \in [2,6]$.

  The integrals in Eq.(13) interested by the change are, in this case, those that having as integration extremes a_i and/or $b_{i-i}(s)$. The change can be expressed as

Accepted to J. Chem. Phys. 10.1063/5.0148175

$$\int_{a_{i-1}}^{b_{i-1}(s)} \tilde{\mathbf{F}}_{i-1}(t)\cdot\tilde{\mathbf{F}}_{i-2}(t-s)dt + \int_{b_{i-1}(s)}^{a_i} \mathbf{F}_{i-1}(t)\cdot\tilde{\mathbf{F}}_{i-2}(t-s)dt + \int_{a_i}^{b_i(s)} \mathbf{F}_i(t)\cdot\tilde{\mathbf{F}}_{i-1}(t-s)dt \tag{20}$$

$$\Downarrow$$

$$\int_{a_{i-1}}^{a_i} \mathbf{F}_{i-1}(t)\cdot\tilde{\mathbf{F}}_{i-2}(t-s)dt + \int_{a_i}^{b_{i-1}(s)} \mathbf{F}_i(t)\cdot\tilde{\mathbf{F}}_{i-2}(t-s)dt + \int_{b_{i-1}(s)}^{b_i(s)} \tilde{\mathbf{F}}_i(t)\cdot\tilde{\mathbf{F}}_{i-1}(t-s)dt \tag{21}$$

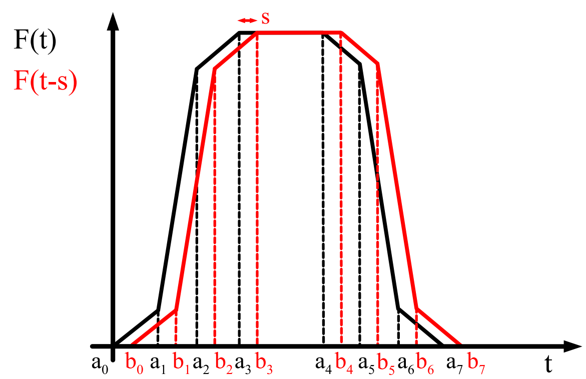

FIG. 2. Graphical representation of a single component of the functions $\mathbf{F}(t)$ (Eq.(3)) and $\mathbf{F}(t-s)$ (Eq.(9)) after a small shift $s \leq s^{(1)}_{i,i-1}$. Different intervals in the time domain are defined by the set $\mathscr{A} \equiv \{a_0, a_1, \cdots, a_7\}$ and $\mathscr{B}(s) \equiv \{b_0(s), b_1(s), \cdots, b_7(s)\}$, respectively.

The $B^{(1)}_{i,i-1}(s)$ quantity is then defined as

$$B^{(1)}_{i,i-1}(s) = \int_{b_{i-1}(s)}^{a_i} \mathbf{F}_{i-1}(t)\cdot\tilde{\mathbf{F}}_{i-2}(t-s)dt + \int_{a_i}^{b_{i-1}(s)} [\mathbf{F}_i(t)\cdot\tilde{\mathbf{F}}_{i-2}(t-s) + \mathbf{F}_{i-1}(t)\cdot\tilde{\mathbf{F}}_{i-1}(t-s)]dt \tag{22}$$

Comparing the relations (20)-(22) with (14)-(19), it follows that the general case $i \in [2,6]$ encompasses the limiting cases $i = 1,7$ recalling that $\mathbf{F}_7 = \tilde{\mathbf{F}}_{-1} = 0$, as already explicitly stated in Eq.(3) and Eq.(9)). Therefore, when $s \gtrsim s^{(1)}_{i,i-1}$, $F_c(s) \equiv A_1(s)$ where

$$A_1(s) = A_0(s) + B^{(1)}_{i,i-1}(s). \tag{23}$$

We now proceed to generalize the procedure outlined here for the first switch, i.e. when s overcomes the value $s^{(1)}_{i,i-1}$ in Eq.(12). In the following we will omit the explicit t, $t-s$ and s from the quantities entering the expression of $F_c(s)$, not to burden the notation.

Let us increase s until one of the term in $\mathscr{B}$, say b_j, becomes equal to one of the elements of $\mathscr{A}$, say a_k, with $k > j$. Hence, this second switch takes place for $s = s^{(2)}_{k,j} = a_k - a_j$. Correspondingly, the changes in the integrals are written as

$$\int_{w_1}^{b_j} \mathbf{F}_{k-1}\cdot\tilde{\mathbf{F}}_{j-1}dt + \int_{b_j}^{a_k} \mathbf{F}_{k-1}\cdot\tilde{\mathbf{F}}_j dt + \int_{a_k}^{w_2} \mathbf{F}_k\cdot\tilde{\mathbf{F}}_j dt$$
$$\Downarrow \tag{24}$$
$$\int_{w_1}^{a_k} \mathbf{F}_{k-1}\cdot\tilde{\mathbf{F}}_{j-1}dt + \int_{a_k}^{b_j} \mathbf{F}_k\cdot\tilde{\mathbf{F}}_{j-1}dt + \int_{b_j}^{w_2} \mathbf{F}_k\cdot\tilde{\mathbf{F}}_j dt$$

where w_1 and w_2 are generic integration extremes belonging to $\mathscr{A}$ or $\mathscr{B}$. Therefore the difference $B^{(2)}_{k,j}$ is expressed by

$$B^{(2)}_{k,j} = \int_{b_j}^{a_k} \mathbf{F}_{k-1}\tilde{\mathbf{F}}_{j-1}dt + \int_{a_k}^{b_j} \Big(\mathbf{F}_k\tilde{\mathbf{F}}_{j-1} + \mathbf{F}_{k-1}\tilde{\mathbf{F}}_j\Big)dt + \int_{b_j}^{a_k} \mathbf{F}_k\tilde{\mathbf{F}}_j dt, \tag{25}$$

which, after straightforward manipulations, becomes

$$B^{(2)}_{k,j} = \int_{b_j}^{a_k} \Big(\mathbf{F}_k - \mathbf{F}_{k-1}\Big)\cdot\Big(\tilde{\mathbf{F}}_j - \tilde{\mathbf{F}}_{j-1}\Big)dt. \tag{26}$$

Thus, the $F_c(s)$ expression for $s \gtrsim s^{(2)}_{kj} = a_k - a_j$ is therefore given by the relation

$$A_2(s) = A_1(s) + B^{(2)}_{k,j}(s). \tag{27}$$

We can iterate this procedure for 28 steps, i.e. the number of switches needed for the equality $b_0 = a_7$ to hold, i.e. $s = t_e$:

$$F_c(s) = \begin{cases} A_0(s) & 0 \leq s \leq s^{(1)}_{i,i-1} \\ A_1(s) = A_0(s) + B^{(1)}_{i,i-1}(s) & s^{(1)}_{i,i-1} \leq s \leq s^{(2)}_{k,j} \\ A_2(s) = A_1(s) + B^{(2)}_{k,j}(s) & s^{(2)}_{k,j} \leq s \leq s^{(3)}_{l,n} \\ \quad\vdots & \quad\vdots \\ A_{27}(s) = A_{26}(s) + B^{(27)}_{p,q}(s) & s^{(27)}_{p,q} \leq s \leq t_e \end{cases} \tag{28}$$

with the constraints that $l > n$ and $p > q$ are the generic indexes relative to the different switches.

Now, by inserting the expression (28) into the definition Eq.(7), after some simplifications we obtain that the NMR attenuation signal becomes

Accepted to J. Chem. Phys. 10.1063/5.0148175

$$
\begin{aligned}
&-\frac{1}{\gamma^2}\ln\frac{S(t_e)}{S(0)} \simeq \int_0^{t_e} A_0(s)C(s)ds+ \\
&\int_{s^{(1)}_{i,i-1}}^{t_e} B^{(1)}_{i,i-1}(s)C(s)ds + \int_{s^{(2)}_{k,j}}^{t_e} B^{(2)}_{k,j}(s)C(s)ds + \cdots + \\
&\int_{s^{(27)}_{p,q}}^{t_e} B^{(27)}_{p,q}(s)C(s)ds.
\end{aligned} \tag{29}
$$

The expression (29) is the central result of our analysis. Indeed, although it may appear rather obscure, it turns out to be very useful and easy to handle for the evaluation of the signal decay. As a matter of fact it makes it possible the evaluation of the signal decay, without a prior knowledge of the exact sequence of the $s^{(n)}_{i,j} = a_i - b_j(s)$ switches, with $i > j$ and $n \in [1,27]$. At the expense of it, all the terms $B^{(n)}_{i,j}$ have to be evaluated for any n and any couple (i,j) (provided the fulfillment of the aforementioned indexes constraints). In the following subsections we will adopt the formula (29) to determine the exact contributions of the terms proportional to $\mathbf{g}^2$, $\mathbf{g}_0^2$ and $\mathbf{g}\cdot\mathbf{g}_0$ for Gaussian processes with stationary increments. The following sections will be devoted to the presentation of practical examples, such as normal (Brownian) and anomalous diffusing processes.

B. Contributions proportional to $\mathbf{g}^2$

The A_0 term of Eq.(29) is obtainable from Eq.(13) after straightforward and tedious calculations. It is easy to see that A_0 is proportional to $\mathbf{g}^2$

$$
\int_0^{\tau_1+\tau_2}\left[\delta^2\left(\Delta-\frac{\delta}{3}\right)+s^2\left(\frac{s}{3}-\delta\right)\right]C(s)ds. \tag{30}
$$

The $\mathbf{g}^2$ contribution due to the $B^{(n)}_{i,j}(s)$ terms is obtained in Appendix (A) (see Eq.(A3)). Summing the term in Eq.(30) to those relative to $B^{(n)}_{i,j}(s)$ as in Eq.(29), the complete $\mathbf{g}^2$ component of Eq.(7) is given by

$$
\begin{aligned}
&\int_0^{\tau_1+\tau_2}\left[\delta^2\left(\Delta-\frac{\delta}{3}\right)+s^2\left(\frac{s}{3}-\delta\right)\right]C(s)ds+ \\
&\frac{1}{3}\int_\delta^{\tau_1+\tau_2}(\delta-s)^3C(s)ds+\frac{1}{6}\int_{\Delta-\delta}^{\tau_1+\tau_2}(\delta-\Delta+s)^3C(s)ds+ \\
&\frac{1}{3}\int_\Delta^{\tau_1+\tau_2}(\Delta-s)^3C(s)ds+\frac{1}{6}\int_{\Delta+\delta}^{\tau_1+\tau_2}(s-\Delta-\delta)^3C(s)ds.
\end{aligned} \tag{31}
$$

C. Contributions proportional to $\mathbf{g}_0^2$

Proceeding analogously to the previous subsection we can firstly calculate the $\mathbf{g}_0^2$ contribution due to A_0

$$
\int_0^{\tau_1+\tau_2}\left[\tau_1^2\left(\tau_2-\frac{\tau_1}{3}\right)+\frac{s^3}{3}-s^2\tau_1\right]C(s)ds. \tag{32}
$$

The term arising from $B^{(n)}_{i,j}(s)$ is calculated in Eq.(A5). Therefore, the total $\mathbf{g}_0^2$ contribution turns out to be

$$
\begin{aligned}
&\int_0^{\tau_1+\tau_2}\left[\tau_1^2\left(\tau_2-\frac{\tau_1}{3}\right)+\frac{s^3}{3}-s^2\tau_1\right]C(s)ds+ \\
&\frac{1}{3}\int_{\tau_1}^{\tau_1+\tau_2}(\tau_1-s)^3C(s)ds+\frac{1}{3}\int_{\tau_2}^{\tau_1+\tau_2}(\tau_2-s)^3C(s)ds+ \\
&\frac{1}{6}\int_{\tau_2-\tau_1}^{\tau_1+\tau_2}(s+\tau_1-\tau_2)^3C(s)ds.
\end{aligned} \tag{33}
$$

D. Contributions proportional to $\mathbf{g}\cdot\mathbf{g}_0$

The coupling term proportional to $\mathbf{g}\cdot\mathbf{g}_0$ is calculated according to the previous subsections. The part of it given by A_0 is

$$
-\delta\int_0^{\tau_1+\tau_2}\left[t_1^2+t_2^2+\delta(t_1+t_2)+\frac{2}{3}\delta^2-2\tau_1\tau_2+2s^2\right]C(s)ds, \tag{34}
$$

where according to the definition of Tanner furnished in[7],

$$
t_2 = \tau_1+\tau_2-(t_1+\Delta+\delta). \tag{35}
$$

The $B^{(n)}_{i,j}(s)$ additive part is furnished in Eq.(A7). By summation, we obtain the final result.

$$
\begin{aligned}
&-\delta\int_0^{\tau_1+\tau_2}[t_1^2+t_2^2+\delta(t_1+t_2)+\frac{2}{3}\delta^2-2\tau_1\tau_2+2s^2]C(s)ds+ \\
&\frac{1}{6}\Big[\int_{t_1}^{\tau_1+\tau_2}(s-t_1)^3C(s)ds+\int_{t_1+\Delta+\delta-\tau_2}^{\tau_1+\tau_2}(t_1+\Delta+\delta-\tau_2-s)^3C(s)ds+ \\
&\int_{t_1+\Delta}^{\tau_1+\tau_2}(t_1+\Delta-s)^3C(s)ds+\int_{\tau_1-t_1}^{\tau_1+\tau_2}(\tau_1-t_1-s)^3C(s)ds+ \\
&\int_{t_1+\Delta+\delta}^{\tau_1+\tau_2}(s-t_1-\Delta-\delta)^3C(s)ds+\int_{\tau_2-t_1}^{\tau_1+\tau_2}(\tau_2-t_1-s)^3C(s)ds+ \\
&\int_{\tau_1-t_1-\delta}^{\tau_1+\tau_2}(t_1+\delta-\tau_1+s)^3C(s)ds+\int_{\tau_2-t_1-\delta}^{\tau_1+\tau_2}(t_1+\delta-\tau_2+s)^3C(s)ds+ \\
&\int_{t_1+\Delta-\tau_1}^{\tau_1+\tau_2}(\tau_1-t_1-\Delta+s)^3C(s)ds+\int_{t_1+\Delta-\tau_2}^{\tau_1+\tau_2}(\tau_2-t_1-\Delta+s)^3C(s)ds+ \\
&\int_{\tau_1+\tau_2-t_1}^{\tau_1+\tau_2}(t_1-\tau_1-\tau_2+s)^3C(s)ds+\int_{t_1+\delta}^{\tau_1+\tau_2}(t_1+\delta-s)^3C(s)ds+ \\
&\int_{t_1+\Delta+\delta-\tau_1}^{\tau_1+\tau_2}(t_1+\Delta+\delta-\tau_1-s)^3C(s)ds+ \\
&\int_{\tau_1+\tau_2-t_1-\delta}^{\tau_1+\tau_2}(\tau_1+\tau_2-t_1-\delta-s)^3C(s)ds+ \\
&\int_{\tau_1+\tau_2-t_1-\Delta}^{\tau_1+\tau_2}(\tau_1+\tau_2-t_1-\Delta-s)^3C(s)ds+ \\
&\int_{\tau_1+\tau_2-t_1-\Delta-\delta}^{\tau_1+\tau_2}(t_1+\Delta+\delta-\tau_1-\tau_2+s)^3C(s)ds\Big].
\end{aligned} \tag{36}
$$

Accepted to J. Chem. Phys. 10.1063/5.0148175

III. NORMAL DIFFUSION

We now want to specify the above general expression for the NMR attenuation signal to the specific case of Brownian diffusion. In this case the spin velocity autocorrelation function is given by[35,41]

$$C(s) = D\zeta e^{-\zeta s} \tag{37}$$

where D is the diffusion coefficient and ζ is the viscous drag characteristic of the system.
Inserting this expression into the Eq.s(31), (33) and into Eq.(36), after explicitly carrying out the integration, we obtain

$$\begin{aligned}
&-\frac{1}{\gamma^2}\ln\frac{S(t_e)}{S(0)} = \mathbf{g}^2\Big\{D\delta^2\Big(\Delta-\frac{\delta}{3}\Big)-\frac{2D}{\zeta^3}\Big[\delta\zeta-1+e^{-\zeta\delta}-\\
&e^{-\zeta\Delta}[\cosh(\zeta\delta)-1]\Big]\Big\}+\mathbf{g}_0^2\Big\{D\tau_1^2\Big(\tau_2-\frac{\tau_1}{3}\Big)-\\
&\frac{2D}{\zeta^3}\Big[\tau_1\zeta-1+e^{-\zeta\tau_1}-e^{-\zeta\tau_2}[\cosh(\zeta\tau_1)-1]\Big]\Big\}+\\
&\mathbf{g}\cdot\mathbf{g}_0\Big\{-D\delta\Big[t_1^2+t_2^2+\delta(t_1+t_2)+\frac{2}{3}\delta^2-2\tau_1\tau_2\Big]-D\frac{4\delta}{\zeta^2}+\\
&\frac{D}{\zeta^3}\Big[e^{-\zeta t_1}-e^{-\zeta(t_1+\delta)}-e^{-\zeta(t_1+\Delta)}+e^{-\zeta(t_1+\Delta+\delta)}-\\
&e^{-\zeta(\tau_1-t_1)}-e^{-\zeta(\tau_2-t_1)}+e^{-\zeta(\tau_1-t_1-\delta)}+e^{-\zeta(\tau_2-t_1-\delta)}+\\
&e^{-\zeta(t_1+\Delta-\tau_1)}-e^{-\zeta(t_1+\Delta+\delta-\tau_1)}+e^{-\zeta(t_1+\Delta-\tau_2)}-\\
&e^{-\zeta(t_1+\Delta+\delta-\tau_2)}+e^{-\zeta(\tau_1+\tau_2-t_1)}+e^{-\zeta(\tau_1+\tau_2-t_1-\delta)}-\\
&e^{-\zeta(\tau_1+\tau_2-t_1-\Delta)}+e^{-\zeta(\tau_1+\tau_2-t_1-\Delta-\delta)}\Big\}
\end{aligned}, \tag{38}$$

where t_2 is given in Eq.(35). This expression constitutes the extension of the PGSTE Tanner formula[7] to the case of diffusing systems with arbitrary ζ. The relation (38) represents the formal exact analytical expression including all the relevant time-scales and physical quantities entering the experimental setup. However, it is of limited practical use if one considers the experimental limits that any NMR apparatus sets. As a matter of fact, the corrections to the Tanner's formula are of the order $\sim \delta\zeta^{-2}$ or $\sim \zeta^{-3}$. Now, if we consider that $10^{-3}sec \lesssim \delta \lesssim 4\cdot 10^{-2}sec$ in modern NMR devices, the value of the damping coefficient ζ becomes crucial in order to estimate the order of magnitude of the corrections. Assuming the validity of the Stoke's formula for a macromolecule diffusing in water, $\zeta = 6\pi r\mu/m$, the water viscosity is $\mu \sim 10^{-3}Pa\cdot s$, the typical macromolecule size is $r \sim 10^{-9}m$ and the mass is $m \sim 10^5 Da$, yielding $\zeta \sim 10^{11}sec^{-1}$. Hence the value of the corrections are many order of magnitude smaller than the leading terms furnished by the original Tanner's formula. Nevertheless, the general theoretical value of the expression (38) remains, suggesting that future technological improvements could allow the direct measurements of the drag coefficient ζ by NMR. On the other side, when $\tau_1 = \tau_2$ and $\zeta, \to \infty$ the PGSE formula is regained[2]. Moreover, when $\mathbf{g}_0 = 0$ we recover the expression furnished in[35].

IV. ANOMALOUS DIFFUSION

The spin velocity autocorrelation function for an anomalous diffusing system, characterized by the Gaussian approximation in the cumulant expansion and stationarity of the increments, is[35]

$$C(s) \sim \alpha(\alpha-1)D_\alpha s^{\alpha-2} \tag{39}$$

where α is the anomalous exponent ($\alpha =\in [0,2]$) and D_α is the generalized diffusion coefficient.
Making use of the expression (39) into the integrals of (31), (33) and into Eq.(36), it is possible to achieve

$$\begin{aligned}
&-\frac{1}{\gamma^2}\ln\frac{S(t_e)}{S(0)} = \mathbf{g}^2\frac{D_\alpha}{(\alpha+2)(\alpha+1)}\Big[(\Delta+\delta)^{\alpha+2}+\\
&(\Delta-\delta)^{\alpha+2}-2\delta^{\alpha+2}-2\Delta^{\alpha+2}\Big]+\mathbf{g}_0^2\frac{D_\alpha}{(\alpha+2)(\alpha+1)}\cdot\\
&\Big[(\tau_1+\tau_2)^{\alpha+2}+(\tau_2-\tau_1)^{\alpha+2}-2\tau_1^{\alpha+2}-2\tau_2^{\alpha+2}\Big]+\\
&\mathbf{g}\cdot\mathbf{g}_0\frac{D_\alpha}{(\alpha+2)(\alpha+1)}\Big[t_1^{\alpha+2}-(t_1+\delta)^{\alpha+2}-(t_1+\Delta)^{\alpha+2}+\\
&(t_1+\Delta+\delta)^{\alpha+2}-(\tau_1-t_1)^{\alpha+2}-(\tau_2-t_1)^{\alpha+2}+\\
&(\tau_1-t_1-\delta)^{\alpha+2}+(\tau_2-t_1-\delta)^{\alpha+2}+(t_1+\Delta-\tau_1)^{\alpha+2}-\\
&(t_1+\Delta+\delta-\tau_1)^{\alpha+2}+(t_1+\Delta-\tau_2)^{\alpha+2}-\\
&(t_1+\Delta+\delta-\tau_2)^{\alpha+2}+(\tau_1+\tau_2-t_1)^{\alpha+2}-\\
&(\tau_1+\tau_2-t_1-\delta)^{\alpha+2}-(\tau_1+\tau_2-t_1-\Delta)^{\alpha+2}+\\
&(\tau_1+\tau_2-t_1-\Delta-\delta)^{\alpha+2}\Big].
\end{aligned} \tag{40}$$

The above equation is the most general form obtainable and can be used to fit any NMR echo signals coming from Gaussian systems displaying anomalous diffusion on the score of stationary increments, when a background gradients is present. To our knowledge it is the first time that a general formulation like this is provided. As a matter of fact it reduces to the normal diffusion case setting $\alpha = 1$. Moreover the PGSE case can be obtained from Eq.(40) putting $\tau_1 = \tau_2$. A handful reduction of it can be gained if we set $t_1 \approx 0$, $\tau_1 \approx \delta$ and $\tau_2 \approx \Delta$. In this case, the Eq.(40) gets the simplified expression

$$\begin{aligned}
&-\frac{1}{\gamma^2}\ln\frac{S(t_e)}{S(0)} = (\mathbf{g}+\mathbf{g}_0)^2\frac{D_\alpha}{(\alpha+2)(\alpha+1)}\cdot\\
&\Big[(\Delta+\delta)^{\alpha+2}+(\Delta-\delta)^{\alpha+2}-2\delta^{\alpha+2}-2\Delta^{\alpha+2}\Big].
\end{aligned} \tag{41}$$

This formula constitutes the natural generalization of the anomalous diffusion expression derived by Karger[45], reported in[46] and rederived by us by different means[35].

V. CONCLUSIONS

We have furnished a comprehensive study of the diffusion weighted NMR signal attenuation in PGSTE-type of experiments, in the presence of a constant background gradient. Our analysis constitutes an alternative approach to the classical Tanner derivation[7]. Our theory considerably extends the range of applicability of the Tanner formula to any systems satisfying the criteria of Gaussianity and stationarity of the increments, and it furnishes the correct analytical way of treating the signals arising from any PFG sequence. In particular we show how our formula can describe any system diffusing normally or anomalous at the microscopic level. We conclude by stressing that the theory developed is valid for any Gaussian system with stationary increments, such as those governed by generalized Langevin equation, fractional Langevin equation or, in general, generalized fractional Langevin equation[47], like single-file systems[48,49] or any other physical process displaying anomalous diffusion on the score of fractional Brownian motion[50].

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Appendix A: Calculation of $B^{(n)}_{i,j}$ terms

To evaluate the quantities in Eq.(29) is convenient to write the terms $\mathbf{F}_i$ and $\tilde{\mathbf{F}}_j$ as generic linear functions respect to t, splitting the $\mathbf{g}_0$ and $\mathbf{g}$ terms in order to point out the different contributions. To this end, considering the Eq.(3) we can write the following general relationships

$$\begin{cases}\mathbf{F}_i &= \mathbf{g}_0(q_{a,i}+m_{a,i}t)+\mathbf{g}(p_{a,i}+r_{a,i}t)\\ \tilde{\mathbf{F}}_j &= \mathbf{g}_0(q_{b,j}+m_{b,j}t)+\mathbf{g}(p_{b,j}+r_{b,j}t)\end{cases} \tag{A1}$$

where the various coefficients are summarized in Table I.

The $\mathbf{g}^2$ contributions of the generic $B^{(n)}_{i,j}$ term can be obtained inserting Eq.(A1) in Eq.(26) obtaining

$$\begin{aligned}&\int_{b_j}^{a_i}\Big(\Delta p_{a,i}+\Delta r_{a,i}t\Big)\Big(\Delta p_{b,j}+\Delta r_{b,j}t\Big)dt=\\ &\frac{1}{6}(a_i-b_j)\Big[6\Delta p_{a,i}\Delta p_{b,j}+3(a_i+b_j)(\Delta p_{a,i}\Delta r_{b,j}+\\ &\Delta r_{a,i}\Delta p_{b,j})+2\Delta r_{a,i}\Delta r_{b,j}(a_i^2+a_ib_j+b_j^2)\Big]\end{aligned} \tag{A2}$$

where $\Delta p_{a,i}\equiv p_{a,i}-p_{a,i-1}$, $\Delta r_{a,i}\equiv r_{a,i}-r_{a,i-1}$ and in an analogous way we define $\Delta p_{b,i}$ and $\Delta r_{b,i}$.
Keeping in mind that $i>j$ and using the parameters in Table I we obtain that the only terms not vanishing are for $(i,j)\in\{(2,1),(5,1),(5,2),(6,1),(6,2),(6,5)\}$. Since $s^n_{ij}=a_i-a_j$ we can write the $B^{(n)}_{ij}$ part as

$$\begin{aligned}&\frac{1}{3}\int_{\delta}^{\tau_1+\tau_2}(\delta-s)^3C(s)ds+\frac{1}{6}\int_{\Delta-\delta}^{\tau_1+\tau_2}(\delta-\Delta+s)^3C(s)ds+\\ &\frac{1}{3}\int_{\Delta}^{\tau_1+\tau_2}(\Delta-s)^3C(s)ds+\frac{1}{6}\int_{\Delta+\delta}^{\tau_1+\tau_2}(s-\Delta-\delta)^3C(s)ds.\end{aligned} \tag{A3}$$

The total $\mathbf{g}^2$ contribution of $F_c(s)$ is obtained summing this result to those one in Eq.(30).
The equation analogous to Eq.(A2) concerning the $\mathbf{g}_0^2$ contribution is

$$\begin{aligned}&\int_{b_j}^{a_i}\Big(\Delta q_{a,i}+\Delta m_{a,i}t\Big)\Big(\Delta q_{b,j}+\Delta m_{b,j}t\Big)dt=\\ &\frac{1}{6}(a_i-b_j)\Big[6\Delta q_{a,i}\Delta q_{b,j}+3(a_i+b_j)(\Delta q_{a,i}\Delta m_{b,j}+\\ &\Delta m_{a,i}\Delta q_{b,j})+2\Delta m_{a,i}\Delta m_{b,j}(a_i^2+a_ib_j+b_j^2)\Big]\end{aligned} \tag{A4}$$

where the various Δ-terms are defined similarly as in Eq.(A2). The terms not vanishing are, in this case, for $(i,j)\in\{(3,0),(4,0),(4,3),(7,3),(7,4)\}$ obtaining the following relative integrals

$$\begin{aligned}&\frac{1}{3}\int_{\tau_1}^{\tau_1+\tau_2}(\tau_1-s)^3C(s)ds+\frac{1}{3}\int_{\tau_2}^{\tau_1+\tau_2}(\tau_2-s)^3C(s)ds+\\ &\frac{1}{6}\int_{\tau_2-\tau_1}^{\tau_1+\tau_2}(s+\tau_1-\tau_2)^3C(s)ds.\end{aligned} \tag{A5}$$

In the end the expression to evaluate the B_{ij} terms for the $\mathbf{g}\cdot\mathbf{g}_0$ is given by

$$\begin{aligned}&\int_{b_j}^{a_i}\Big(\Delta q_{a,i}+\Delta m_{a,i}t\Big)\Big(\Delta p_{b,j}+\Delta r_{b,j}t\Big)dt+\\ &\int_{b_j}^{a_i}\Big(\Delta p_{a,i}+\Delta r_{a,i}t\Big)\Big(\Delta q_{b,j}+\Delta m_{b,j}t\Big)dt=\\ &\frac{1}{6}(a_i-b_j)\Big[6(\Delta q_{a,i}\Delta p_{b,j}+\Delta p_{a,i}\Delta q_{b,j})+3(a_i+b_j)\cdot\\ &(\Delta q_{a,i}\Delta r_{b,j}+\Delta m_{a,i}\Delta p_{b,j}+\Delta p_{a,i}\Delta m_{b,j}+\Delta r_{a,i}\Delta q_{b,j})+\\ &2(\Delta m_{a,i}\Delta r_{b,j}+\Delta r_{a,i}\Delta m_{b,j})(a_i^2+a_ib_j+b_j^2)\Big].\end{aligned} \tag{A6}$$

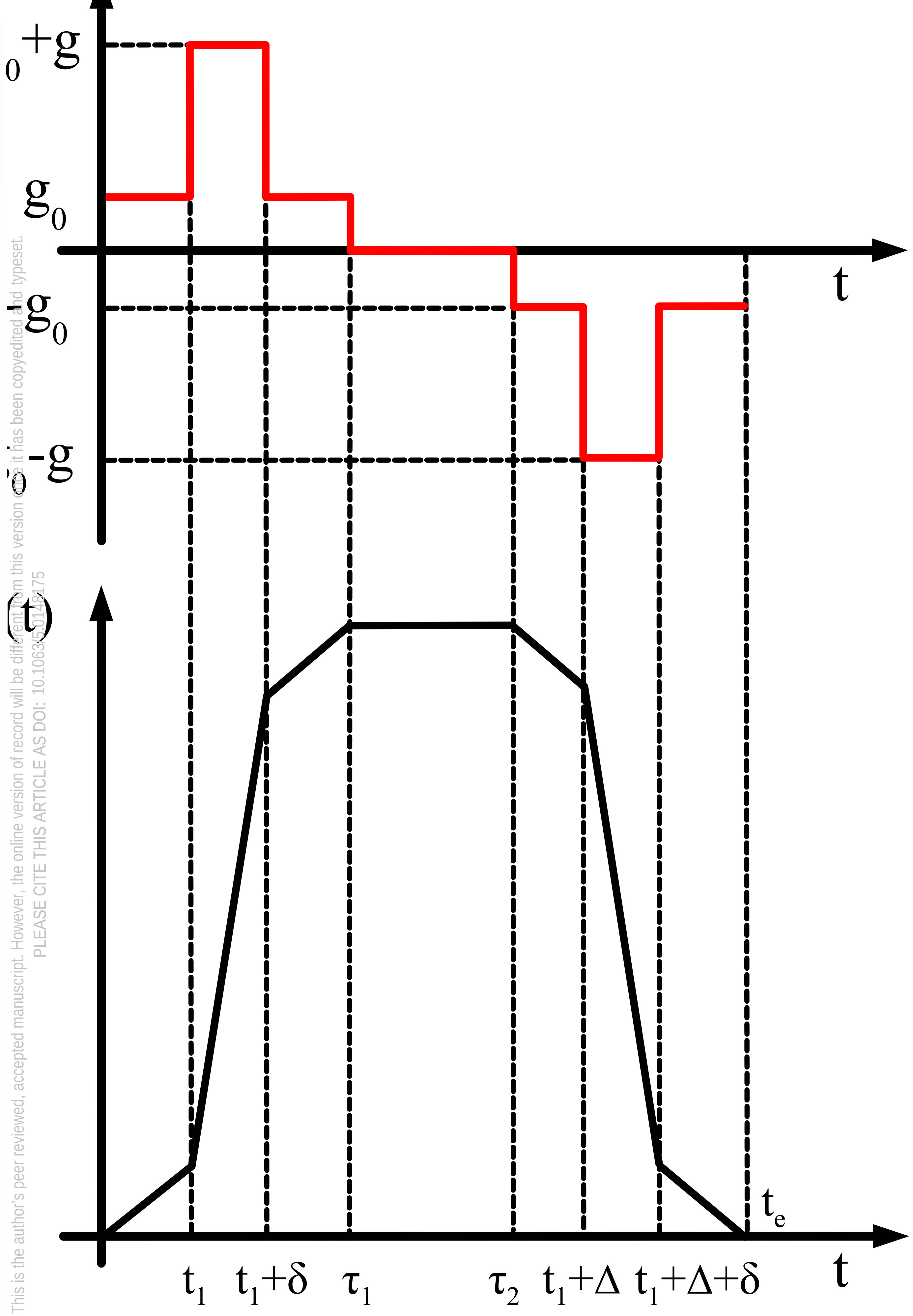
From this equation we get that the indexes useful are $(i,j)\in\{(1,0),(2,0),(5,0),(6,0),(3,1),(4,1),(7,1),(3,2),(4,2),(7,2),(5,3),(6,3),(5,4),(6,4),(7,5),(7,6)\}$ and the $B_{i,j}$ contributions are

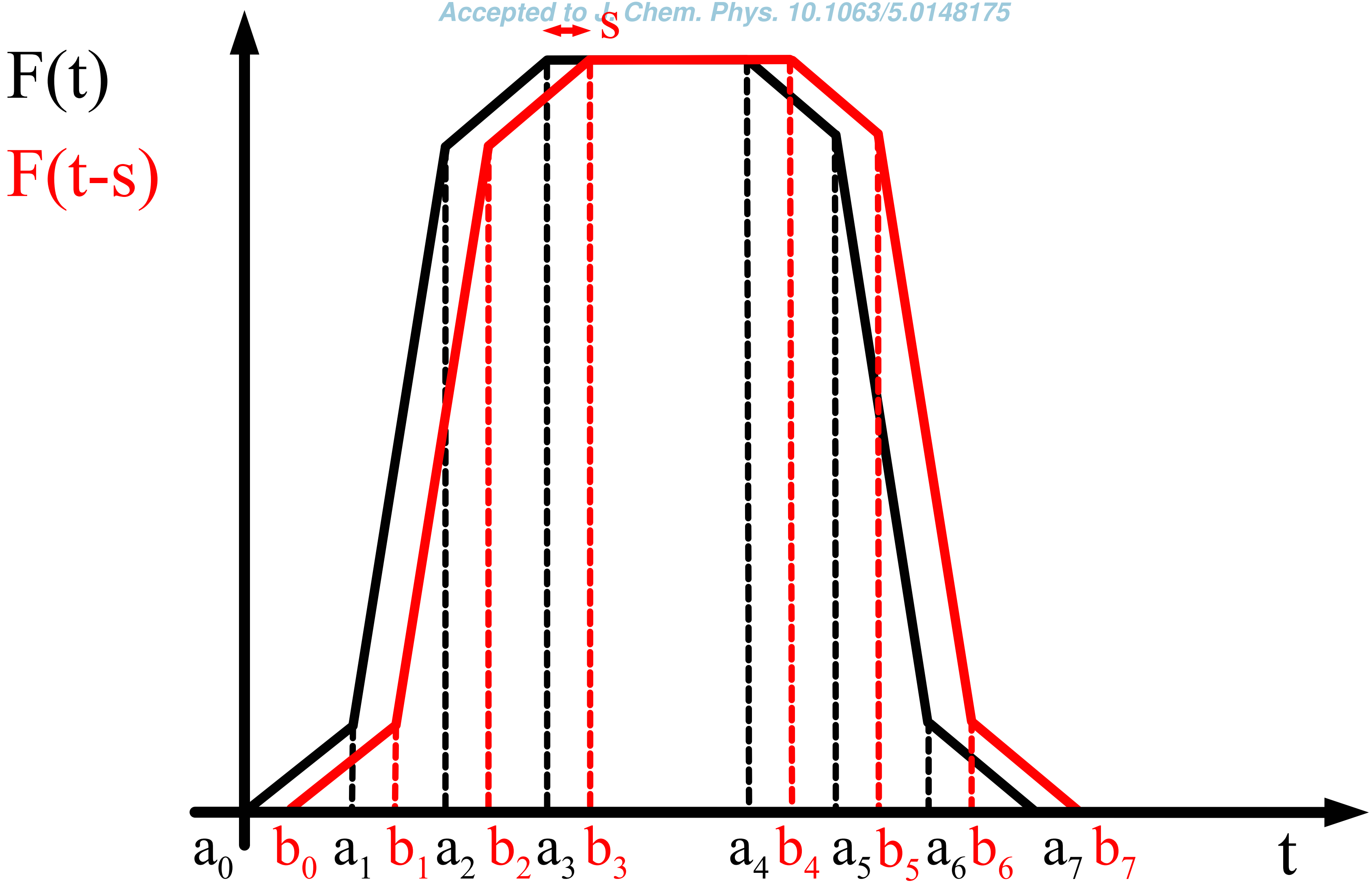
Accepted to J. Chem. Phys. 10.1063/5.0148175

$$\frac{1}{6}\Big[\int_{t_1}^{\tau_1+\tau_2}(s-t_1)^3C(s)ds+\int_{t_1+\delta}^{\tau_1+\tau_2}(t_1+\delta-s)^3C(s)ds+\int_{t_1+\Delta}^{\tau_1+\tau_2}(t_1+\Delta-s)^3C(s)ds+\int_{\tau_1-t_1}^{\tau_1+\tau_2}(\tau_1-t_1-s)^3C(s)ds+$$
$$\int_{t_1+\Delta+\delta}^{\tau_1+\tau_2}(s-t_1-\Delta-\delta)^3C(s)ds+\int_{\tau_2-t_1}^{\tau_1+\tau_2}(\tau_2-t_1-s)^3C(s)ds+\int_{\tau_1-t_1-\delta}^{\tau_1+\tau_2}(t_1+\delta-\tau_1+s)^3C(s)ds+\int_{\tau_2-t_1-\delta}^{\tau_1+\tau_2}(t_1+\delta-\tau_2+s)^3C(s)ds+$$
$$\int_{t_1+\Delta-\tau_1}^{\tau_1+\tau_2}(\tau_1-t_1-\Delta+s)^3C(s)ds+\int_{t_1+\Delta+\delta-\tau_1}^{\tau_1+\tau_2}(t_1+\Delta+\delta-\tau_1-s)^3C(s)ds+\int_{t_1+\Delta-\tau_2}^{\tau_1+\tau_2}(\tau_2-t_1-\Delta+s)^3C(s)ds+ \tag{A7}$$
$$\int_{t_1+\Delta+\delta-\tau_2}^{\tau_1+\tau_2}(t_1+\Delta+\delta-\tau_2-s)^3C(s)ds+\int_{\tau_1+\tau_2-t_1}^{\tau_1+\tau_2}(t_1-\tau_1-\tau_2+s)^3C(s)ds+\int_{\tau_1+\tau_2-t_1-\delta}^{\tau_1+\tau_2}(\tau_1+\tau_2-t_1-\delta-s)^3C(s)ds+$$
$$\int_{\tau_1+\tau_2-t_1-\Delta}^{\tau_1+\tau_2}(\tau_1+\tau_2-t_1-\Delta-s)^3C(s)ds+\int_{\tau_1+\tau_2-t_1-\Delta-\delta}^{\tau_1+\tau_2}(t_1+\Delta+\delta-\tau_1-\tau_2+s)^3C(s)ds\Big].$$

	$q_{a,i}$	$m_{a,i}$	$p_{a,i}$	$r_{a,i}$		$q_{b,j}$	$m_{b,j}$	$p_{b,j}$	$r_{b,j}$
$i=0$	0	1	0	0	$j=0$	$-s$	1	0	0
$i=1$	0	1	$-t_1$	1	$j=1$	$-s$	1	$-t_1-s$	1
$i=2$	0	1	δ	0	$j=2$	$-s$	1	δ	0
$i=3$	τ_1	0	δ	0	$j=3$	τ_1	0	δ	0
$i=4$	$\tau_1+\tau_2$	-1	δ	0	$j=4$	$\tau_1+\tau_2+s$	-1	δ	0
$i=5$	$\tau_1+\tau_2$	-1	$t_1+\Delta+\delta$	-1	$j=5$	$\tau_1+\tau_2+s$	-1	$t_1+\Delta+\delta+s$	-1
$i=6$	$\tau_1+\tau_2$	-1	0	0	$j=6$	$\tau_1+\tau_2+s$	-1	0	0

TABLE I. Coefficients of Eq.(A1)


0 +g
g0
t
g0
-g
(t)
t1
t1+δ
τ1
τ2
t1+Δ
t1+Δ+δ
te
t



F(t)
F(t-s)
s
a0 b0 a1 b1 a2 b2 a3 b3 a4 b4 a5 b5 a6 b6 a7 b7
t