139 (2014) MATHEMATICA BOHEMICA No. 2, 155–162

TIME DELAY IN CHEMICAL EXCHANGE DURING AN NMR PULSE

Dan Gamliel, Ariel

(Received September 15, 2013)

Abstract. Spin exchange with a time delay in NMR (nuclear magnetic resonance) was treated in a previous work. In the present work the idea is applied to a case where all magnetization components are relevant. The resulting DDE (delay differential equations) are formally solved by the Laplace transform. Then the stability of the system is studied using the real and imaginary parts of the determinant in the characteristic equation. Using typical parameter values for the DDE system, stability is shown for all relevant cases. Also non-oscillating terms in the solution were found by studying the same determinant using similar parameter values.

Keywords: magnetic resonance; spin exchange; delay differential equation; characteristic equation

MSC 2010: 11C20, 34K06, 34C26

1. Introduction

Spin (or "chemical") exchange processes are studied via their effect on the NMR spectrum of a given spin system [8], [2]. In a previous work we considered an exchange process with a time delay, but only the z-component of magnetization was relevant [3], [4], [5]. The system was described by the Bloch-McConnell equations with a time delay, and the number of equations was equal to the number of exchanging sites.

In this work the exchange process occurs during the rf pulse, before saturation is reached [11], so that all three components of the magnetization are coupled. The delay in the exchange process leads to a set of DDE. The Laplace transform is used below to get a formal solution, and then the characteristic equation is used to obtain results about the stability and about non-oscillating terms in the solution.

2. Delayed exchange during a pulse

The Bloch-McConnell equations for the magnetization with delay in the exchange process between sites α, β are (for $t > 0$)

$$\frac{\mathrm{d}}{\mathrm{d}t}\mathbf{x}(t) + \mathbf{A}\cdot\mathbf{x}(t) + \mathbf{B}\cdot\mathbf{x}(t-\tau) = \mathbf{u}. \tag{2.1}$$

For earlier time values a preshape function has to be assumed:

$$\mathbf{x}(t) = \varphi(t) \quad \text{for} \quad 0 > t > -\tau \tag{2.2}$$

and for $t = 0$ the initial condition is:

$$\mathbf{x}(0) = \mathbf{x_0}. \tag{2.3}$$

The vectors in Equation (2.1) are the vector of time dependent magnetization

$$\mathbf{x} = \begin{pmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \\ x_6 \end{pmatrix} = \begin{pmatrix} M_{x\alpha} \\ M_{y\alpha} \\ M_{z\alpha} \\ M_{x\beta} \\ M_{y\beta} \\ M_{z\beta} \end{pmatrix} \tag{2.4}$$

and the vector of equilibrium values of the magnetization

$$\mathbf{u} = \begin{pmatrix} 0 \\ 0 \\ R_{1\alpha}\cdot M_{0\alpha} \\ 0 \\ 0 \\ R_{1\beta}\cdot M_{0\beta} \end{pmatrix}. \tag{2.5}$$

The pre-shape function and the initial condition are assumed equal to the equilibrium vector $\mathbf{u}$. The matrices are

$$\mathbf{A} = \begin{pmatrix} R_{2\alpha}+k_{\alpha\beta} & \Delta_\alpha & 0 & 0 & 0 & 0 \\ -\Delta_\alpha & R_{2\alpha}+k_{\alpha\beta} & -\omega_1 & 0 & 0 & 0 \\ 0 & \omega_1 & R_{1\alpha}+k_{\alpha\beta} & 0 & 0 & 0 \\ 0 & 0 & 0 & R_{2\beta}+k_{\beta\alpha} & \Delta_\beta & 0 \\ 0 & 0 & 0 & -\Delta_\beta & R_{2\beta}+k_{\beta\alpha} & -\omega_1 \\ 0 & 0 & 0 & 0 & \omega_1 & R_{1\beta}+k_{\beta\alpha} \end{pmatrix}, \tag{2.6}$$

$$\mathbf{B} = \begin{pmatrix} 0 & 0 & 0 & -k_{\beta\alpha} & 0 & 0 \\ 0 & 0 & 0 & 0 & -k_{\beta\alpha} & 0 \\ 0 & 0 & 0 & 0 & 0 & -k_{\beta\alpha} \\ -k_{\alpha\beta} & 0 & 0 & 0 & 0 & 0 \\ 0 & -k_{\alpha\beta} & 0 & 0 & 0 & 0 \\ 0 & 0 & -k_{\alpha\beta} & 0 & 0 & 0 \end{pmatrix}. \tag{2.7}$$

In these equations: for site ξ ($\xi = \alpha, \beta$), $R_{1\xi} = 1/T_{1\xi}$ and $R_{2\xi} = 1/T_{2\xi}$ are the longitudinal and transversal relaxation rates, respectively, $\Delta_\xi = \omega - \omega_{0\xi}$ is the pulse off-resonance, $M_{0\xi}$ is its equilibrium magnetization (proportional to its population), ω_1 is the pulse amplitude and $k_{\xi\psi}$ is the jump rate from site ξ to site ψ.

Detailed balance implies: $k_{\alpha\beta} \cdot M_{0\alpha} = k_{\beta\alpha} \cdot M_{0\beta}$. In typical applications one site is in bulk (free) water in the tissue and the other site is bound to a large molecule, so $M_{0\alpha} \gg M_{0\beta}$. Therefore $k_{\alpha\beta} = m \cdot k_{\beta\alpha} \ll k_{\beta\alpha}$ where $m \equiv M_{0\beta}/M_{0\alpha} \ll 1$. From this point the shorter notation $k = k_{\beta\alpha}$ will be used.

3. Formal Laplace transform of the equation

Applying the Laplace transform to the equilibrium vector results in

$$U(s) = \int_0^\infty \mathrm{e}^{-s\cdot\tau} u \,\mathrm{d}t = \frac{1}{s} \cdot u. \tag{3.1}$$

The pre-shape function is transformed as

$$\Phi(s) = \int_0^\tau \mathrm{e}^{-s\cdot\tau} \varphi(t-\tau) \,\mathrm{d}t = \frac{1}{s} \cdot (1 - \mathrm{e}^{-s\cdot\tau}) \cdot u. \tag{3.2}$$

Using the definition $X(s) = \int_0^\infty \mathrm{e}^{-s\cdot\tau} x(t) \,\mathrm{d}t$, Equation (2.1) is transformed to

$$s \cdot X(s) - x(0) + \mathbf{A} \cdot X(s) + \mathbf{B} \cdot \{\Phi(s) + \mathrm{e}^{-s\cdot\tau} \cdot X(s)\} = U(s). \tag{3.3}$$

Therefore

$$X(s) = \{s \cdot \mathbf{I} + \mathbf{A} + \mathrm{e}^{-s\cdot\tau} \cdot \mathbf{B}\}^{-1} \cdot \{x(0) - \mathbf{B} \cdot \Phi(s) + U(s)\} \tag{3.4}$$

where $\mathbf{I}$ is the identity matrix. Now define the characteristic (matrix) function

$$H(s) = s \cdot \mathbf{I} + \mathbf{A} + \mathrm{e}^{-s\cdot\tau} \cdot \mathbf{B}. \tag{3.5}$$

Using this definition, the formal solution in the space of s-variable is

$$X(s) = \{H(s)\}^{-1} \cdot \left\{ \left(1 + \frac{1}{s}\right) \cdot u - \mathbf{B} \cdot \frac{1}{s}(1 - \mathrm{e}^{-s\cdot\tau}) \cdot u \right\}. \tag{3.6}$$

For the inversion of the characteristic matrix, if a matrix $\mathbf{C}$ is a "partitioned matrix",

$$\mathbf{C} = \begin{pmatrix} C_{11} & C_{12} \\ C_{21} & C_{22} \end{pmatrix} \tag{3.7}$$

where each "element" is a sub-matrix, then its inverse has a similar structure

$$\mathbf{C}^{-1} = \mathbf{D} = \begin{pmatrix} D_{11} & D_{12} \\ D_{21} & D_{22} \end{pmatrix} \tag{3.8}$$

with the following expressions for its sub-matrices [6]:

$$\begin{aligned} D_{11} &= (C_{11} - C_{12} \cdot C_{22}^{-1} \cdot C_{21})^{-1}, \\ D_{12} &= -D_{11} \cdot C_{12} \cdot C_{22}^{-1}, \\ D_{21} &= -C_{22}^{-1} \cdot C_{21} \cdot D_{11}, \\ D_{11} &= C_{22}^{-1} + C_{22}^{-1} \cdot C_{21} \cdot D_{11} \cdot C_{12} \cdot C_{22}^{-1}. \end{aligned} \tag{3.9}$$

In $H(s)$ two sub-matrices are proportional to the identity matrix: $C_{12} = -k\mathrm{e}^{-s\tau} \cdot \mathbf{I}$ and $C_{21} = -m \cdot k\mathrm{e}^{-s\tau} \cdot \mathbf{I}$. From Equation (3.9) one obtains explicit expressions for $H(s)^{-1}$ where each matrix element is a ratio of two exponential polynomials, each of the form

$$\sum_{0 \leqslant i \leqslant 6} \sum_{0 \leqslant j \leqslant 6} c_{ij} s^i \mathrm{e}^{-j \cdot s \cdot \tau}. \tag{3.10}$$

The inverse Laplace transform of $X(s)$ can be calculated using complex residues of such expressions. However, due to their complexity it is desirable to have an alternative method to study the solution of Equation (2.1).

4. Studying the solution by the characteristic equation

The roots of the characteristic equation are fundamental to studying the original DDE [1]. The characteristic equation here is

$$h(s) = \det(H(s)) = \det(s \cdot \mathbf{I} + \mathbf{A} + \mathrm{e}^{-s\cdot\tau} \cdot \mathbf{B}) = 0. \tag{4.1}$$

Equation (2.1) has an infinite number of roots, arranged asymptotically in "root chains" [1]. From the form of Equation (2.1) Theorem 12.12 of [1] applies, and all root chains are "retarded", i.e., for root s: $|s| \to \infty \Rightarrow \mathrm{Re}(s) \to -\infty$. For the initial conditions chosen, also Theorem 6.5 of [1] holds, so that for $t > n\tau$, where n is the dimension of the problem ($n = 6$ in our case), the solution of Equation (2.1) is of the form

$$x(t) = \lim_{j \to \infty} \sum_{C_j} \mathrm{e}^{s_r \cdot t} p_r(t) \tag{4.2}$$

where $p_r(t)$ is a vector polynomial and s_r is a root of $h(s)$ (see details in [1]). From this expression one can study the stability and purely decaying terms in the solution (most roots occur in complex conjugate pairs, leading to decay with oscillations).

4.1. The stability of the system. The main result relevant here is Theorem 13.7 of [1]. When the determinant $h(s)$ is evaluated on the imaginary axis: $s = \mathrm{i}y$ (real y), the result is written as $h(s) = f(s)+\mathrm{i}g(s)$ (real valued $f(s), g(s)$). Part of the theorem is the following statement:

In order that all the zeros of this function lie to the left of the imaginary axis, it is sufficient that all the zeros of the functions $f(s)$, $g(s)$ be real and alternate and the inequality

$$g'(y) \cdot f(y) - g(y) \cdot f'(y) > 0 \tag{4.3}$$

hold at least for one value of y.

Having "alternate roots" means that neither function has a multiple zero, that between every two zeros of one function there is at least one zero of the other, and the functions have no common zero. These conditions guarantee stability of the solution. The behavior of $h(s)$ was studied on the imaginary axis with the auxiliary definition [1]:

$$P(s) = \mathrm{e}^{s\cdot\tau} \cdot H(s) \quad \Rightarrow \quad p(s) = \det(P(s)) = \mathrm{e}^{N\cdot s\cdot\tau} \cdot h(s) \tag{4.4}$$

where $N = 6$ is the dimension of the matrix $H(s)$. Clearly $p(s)$ and $h(s)$ have the same zeros. The calculation of the determinant is simplified by noting that for a matrix $\mathbf{C}$ with the structure as in Equation (3.7) the determinant is [7]

$$\det(\mathbf{C}) = \det(C_{11}) \cdot \det(C_{22} - C_{21} \cdot C_{11}^{-1} \cdot C_{12}). \tag{4.5}$$

The resulting expression was evaluated numerically with the following parameters (similar to typical experimental values):

$$R_{1\alpha} = R_{1\beta} = R_{2\alpha} = R_{2\beta} = 1\,\mathrm{s}^{-1}, \quad \omega_1 = 2\pi \cdot 600 = 3770\,\mathrm{s}^{-1},$$
$$k = 1000\,\mathrm{s}^{-1},\ m = 0.001, \quad \Delta_\beta = 0,\ \Delta_\alpha = \Delta_\beta - 2\pi \cdot 20.000 = -125664\,\mathrm{s}^{-1}.$$

It is known that the average lifetime of a state is equal to $T = 1/k$ where k is the jump (exchange) rate from this state. Thus to study the effect of delay on the system, the calculation was done for the following three cases:

a) Short delay: $\tau = (0.1) \cdot 1/k$ ($\tau \ll T$).

b) Intermediate delay: $\tau = 1/k$ ($\tau = T$).

c) Long delay: $\tau = (10.) \cdot 1/k$ ($\tau \gg T$).

The inequality (4.3) was checked for all cases for $-100 \leqslant y \leqslant 100$, and it holds everywhere. The computed $h(s)$ for all cases corresponds to the conditions of the theorem (Figures 1–3). Thus in all cases the system is stable.

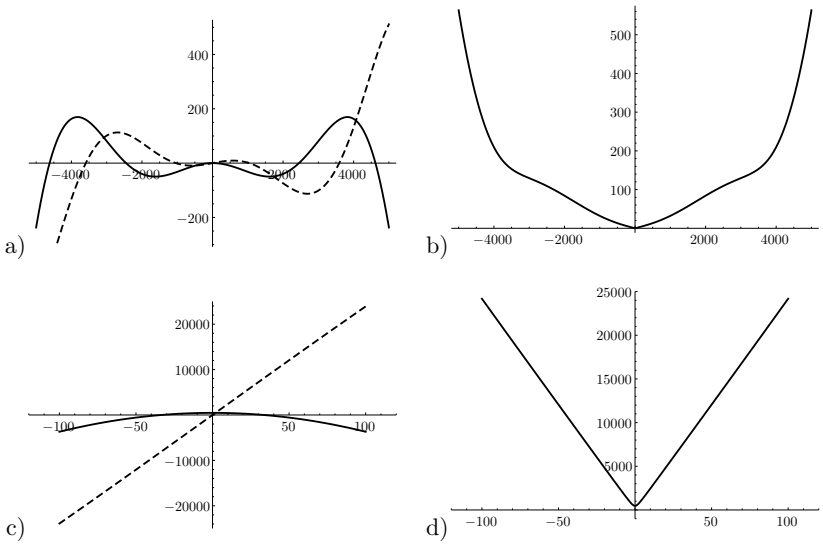

Figure 1. Values of $h(s = \mathrm{i}y)$ (vert., in arb. units) for: $\tau = (0.1) \cdot 1/k$, as a function of $y = \mathrm{Im}(s)$ (horiz.); a) $\mathrm{Re}(h(s))$ (solid) and $\mathrm{Im}(h(s))$ (dashed); b) $\mathrm{Abs}(h(s))$; c) expanded view, center of a); d) expanded view, center of b).

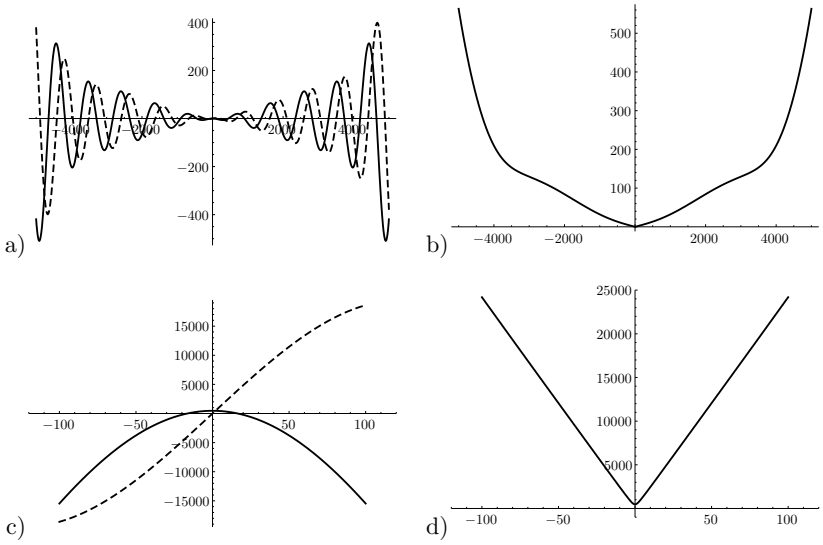

Figure 2. Values of $h(s = \mathrm{i}y)$ for: $\tau = 1/k$, as a function of $y = \mathrm{Im}(s)$; a)–d) as in Figure 1.

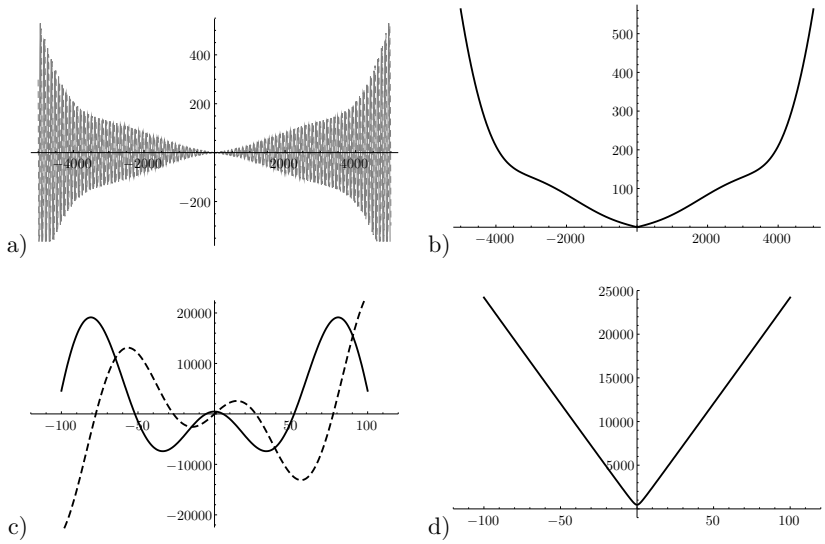

Figure 3. Values of $h(s = \mathrm{i}y)$ for: $\tau = (10.) \cdot 1/k$, as a function of $y = \mathrm{Im}(s)$; a)–d) as in Figure 1.

4.2. Non-oscillating terms in the solution. In order to find non-oscillating terms in the solution it is possible to use general algorithms for searching in the complex plane the roots of $h(s)$ ([9], [10], [12]). However, it is simpler to compute directly the value of $h(s)$ (or $p(s)$ as in Equation (4.4)) on the real axis, and since the system is stable, it is sufficient to look at the negative half of the real axis. The computation of $p(s)$ (which is real on the real axis) was done for all three cases (see next page Figure 4), and roots were found, showing the decay constants of the non-oscillating terms.

Summarizing, for typical parameter values of the system the equations were found to be stable for any value of the delay time. Non-oscillating terms were found for all cases, with a very slight dependence of the decay rate on the delay value, except for very long delay where the faster decaying term does not appear.

References

[1] *R. Bellman, K. L. Cooke*: Differential-Difference Equations. Mathematics in Science and Engineering 6, Academic Press, New York, 1963. zbl MR

[2] *D. Gamliel, H. Levanon*: Stochastic Processes in Magnetic Resonance. World Scientific, Singapore, 1995.

[3] *D. Gamliel*: Generalized exchange in magnetic resonance. Funct. Differ. Equ. *18* (2011), 201–227.

[4] *D. Gamliel*: Using the Lambert function in an exchange process with a time delay. Electron. J. Qual. Theory Differ. Equ. Proc. 9th Coll. QTDE *7* (2012), 1–12.

[5] *D. Gamliel, A. Domoshnitsky, R. Shklyar*: Time evolution of spin exchange with a time delay. Funct. Differ. Equ. *20* (2013), 81–113.

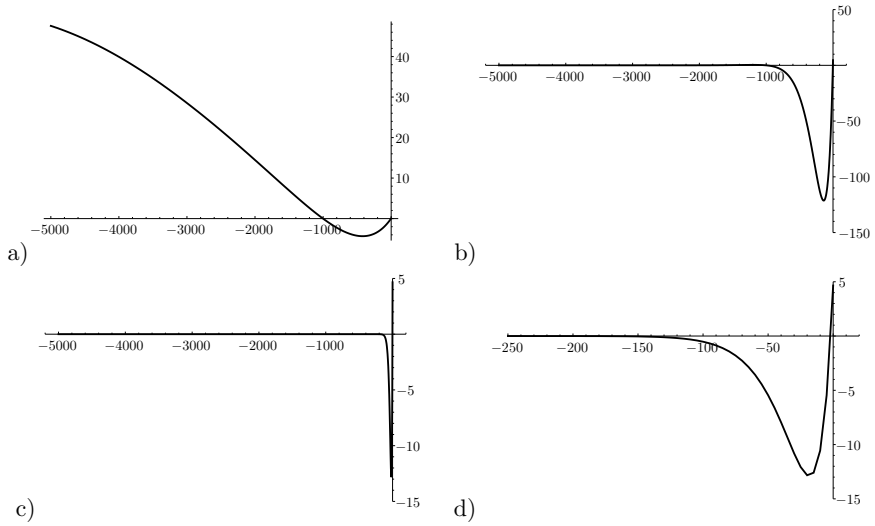

Figure 4. Values of $p(s)$ on the real axis ($s = x$), as a function of x; a) for $\tau = (0.1) \cdot 1/k$, the roots are: $s = -1.929$ and $s = -1001.006$; b) for $\tau = 1/k$, the roots are: $s = -1.933$ and $s = -1001.012$; c) for $\tau = (10.) \cdot 1/k$, the only root is: $s = -1.931$ (for $s < -1000$ $p(s)$ is very close to zero); d) expanded view, center of c).

[6] *G. Hadley*: Linear Algebra. Addison-Wesley Series in Industrial Management, Addison Wesley Publishing Company, Reading, 1961. zbl MR

[7] *R. A. Horn, C. R. Johnson*: Matrix Analysis. (2nd ed.), Cambridge University Press, Cambridge, 2013. zbl MR

[8] *J. I. Kaplan, G. Fraenkel*: NMR of Chemically Exchanging Systems. Academic Press, New York, 1980.

[9] *K. Verheyden, T. Luzyanina, D. Roose*: Efficient computation of characteristic roots of delay differential equations using LMS methods. J. Comput. Appl. Math. *214* (2008), 209–226. zbl MR

[10] *T. Vyhlídal, P. Zítek*: Mapping based algorithm for large scale computation of quasi-polynomial zeros. IEEE Trans. Autom. Control *54* (2009), 171–177. MR

[11] *D. E. Woessner, S. Zhang, M. E. Merritt, A. D. Sherry*: Numerical solutions of the Bloch equations provides insights into the optimum design of PARACEST agents for MRI. Mag. Reson. Med. *53* (2005), 790–799.

[12] *Z. Wu, W. Michiels*: Reliably computing all characteristic roots of delay differential equations in a given right half plane using a spectral method. J. Comput. Appl. Math. *236* (2012), 2499–2514. zbl MR

Author's address: *Dan Gamliel*, Department of Physics, Ariel University, Kiryat Hamada, Ariel 40700, Israel, e-mail: `dang@ariel.ac.il`.