Communication

Structural properties of 2D NMR relaxation spectra of diffusive systems

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ABSTRACT

Much has been learnt and speculated about the form of 2D NMR relaxation spectra of diffusive systems. Herein we show that the eigen-modes formalism can help to establish a number of fundamental structural properties, i.e. symmetries, overall intensities, signs and relative intensities of the diagonal and cross components, of such spectra, on which one can safely rely in analysing experimental data. More specifically, we prove that the correlation T_1–T_2 spectra will always have negative peaks, thus making questionable the nowadays wide spread strategy in developing inverse Laplace transformation algorithms.

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1. Introduction

The development of two-dimensional (2D) relaxation techniques is one of the major advances in NMR over the last ten years. Correlating various relaxation mechanisms rather than Larmor frequencies and chemical shifts, these techniques provide new scope for the use of ideas originating in the multi-dimensional Fourier Transformation (FT) spectroscopy [1]. Numerous heterogeneous systems can't be studied by the FT spectroscopy either because their spectra are of no interest or because the acquisition of the latter is hindered by the intrinsic inhomogeneity in magnetic susceptibility. Relaxation rates can turn out extremely valuable to identify different constituents or various compartments in such systems [2]. This is the case of confined fluids in porous media, in which relaxation rates can be related direct to the pore sizes [3]; foods, in which various ingredients have distinct relaxation rates [4]; or complex fluids, such as cements during its setting, in which the measurement of relaxation rates allows to monitor the formation of organised structures [5]. Since the late 1980s, one-dimensional (1D) Inverse Laplace Transformation (ILT) spectroscopy has allowed observation of relaxation rate distributions in various materials [6].

Nowadays the 2D ILT spectroscopy, correlating various processes that drive relaxation, holds out hope of more in-depth understanding of composition and dynamics of those materials. Unlike the FT spectroscopy, its ILT counterpart is also of great interest for those NMR studies where only spectrometers with an externalised magnet, RF transmitter and receiver coils must be used, e.g.

NMR-Mouse [7] or GarField [8]. Both types of spectroscopy saw the light three decades ago or so [9,10]. Constant progress has been made in the FT spectroscopy ever since, while the early development of the ILT spectroscopy was relatively slow. The reason for this was, as their mere names suggest, that one type of spectroscopy relies on the FT of raw NMR data collected in experiments as a function of the time, while the other necessitates the ILT of the data. The numerical implementation of the multidimensional FT never posed any fundamental problem. On the contrary, performing the multidimensional ILT numerically had long been a formidable task and one had to wait until 2002 to see the first 2D ILT algorithm that could be run on an ordinary PC [11,12]. This was followed by the development of several rather straightforward NMR experimental schemes, viz. the T_1–T_2 correlation [11,12], where a period of spin–spin relaxation follows a period of spin–lattice relaxation, thus correlating the spin–lattice and spin–spin relaxation rates; the T_2–T_2 correlation [13], where two periods of spin–spin relaxation are separated by a period of fixed duration during which the spin system is subject to spin–lattice relaxation, and which correlates the spin–spin relaxation rates with themselves; as well as the T_1–T_1 correlation [14], where spin–lattice relaxation rates are correlated with themselves, and where a period of fixed duration during which the spin system is subject to spin–spin relaxation is sandwiched between two periods of spin–lattice relaxation.

Study of various systems have already benefited from the 2D ILT spectroscopy, viz. polymers [7], fruits and vegetables [15], cement-based materials [8], as well as water and oil in rocks [16]. The relaxation rates T_1 and T_2 are sometimes completed by other information, such as molecular diffusion [17] or chemical shifts [14]. The ratio T_1/T_2 – a key element in the relaxation analysis- could be determined direct from correlation spectra T_1–T_2 [13].

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Observation of cross-peaks in correlation spectra of cements was the first experimental proof that water migrates between certain types of pore [13]. Systematic studies of those peaks allow to measure chemical exchange rates between particular sites [18].

Nevertheless, assignment of various components and interpretation of 2D spectra encountered in ILT spectroscopy is still difficult [19], as they are subject to defects introduced by the 2D ILT programmes available to date. These defects, described in literature [20], consist in each of the large components of the spectrum bursting into a number of smaller peaks as well as in appearing spurious peaks. Furthermore, the present algorithm was designed on a premise that all the components of a spectrum have positive amplitudes. Recent theoretical studies, though, showed spectra containing peaks of both signs [21,22]. Thus, a mathematically rigorous study of the structure of 2D spectra correlating various relaxation rates could, we believe, considerably benefit the future analysis of experimental data.

Two approaches have been used in the modelling of relaxation spectra. One of them, largely inspired by the first-order two-site exchange model [21], has allowed to analyse quantitatively spectra of numerous systems, but turned out much too specific to permit by its self to thoroughly understand the fundamental structural features of the spectra. Another one [22], based on the eigen-modes formalism, is much more general, but, being rather abstract, has not attracted enough spectroscopists' attention. In this report, we show that within this latter formalism a wealth of useful structural properties of the spectra can be expressed in a mathematically rigorous way.

2. Theory

2.1. Diffusive systems

Being placed in the magnet of an NMR spectrometer, porous media and live tissues can be regarded as diffusive systems, in which local magnetisation $m(\mathbf{r})$ stems essentially from an interstitial fluid – often water or oil – free to diffuse in pores. The magnetisation density difference from its equilibrium value satisfies the equation

$$\phi(\mathbf{r})\frac{\partial m}{\partial t} = \nabla(\mathbf{D}(\mathbf{r})\nabla m) - \phi(\mathbf{r})\mu_\alpha(\mathbf{r})m \tag{1}$$

where $\phi(\mathbf{r})$, $\mathbf{D}$ and μ_α stand for the local concentration of the fluid, diffusion tensor and relaxation rate, respectively [2]. The subscript $\alpha = 1$ or 2, depending on whether it deals with spin–lattice or spin–spin relaxation. At the surface between the fluid and solid phases of the system, the relaxation rate ρ_α may be much higher than that μ_α inside the fluid. It is governed by the boundary condition

$$\mathbf{n}(\mathbf{r}) \cdot \mathbf{D}(\mathbf{r})\nabla m = \phi(\mathbf{r})\rho_\alpha(\mathbf{r})m \tag{2}$$

where $\mathbf{n}$ is the normal unit vector directed towards the inside of the fluid phase.

2.2. Eigen-modes formalism

This system has orthonormal bases of spin–lattice $|\Psi_{1,n}(\mathbf{r})\rangle$ and spin–spin $|\Psi_{2,n}(\mathbf{r})\rangle$ relaxation eigen-states with real relaxation eigen-times $\tau_{1,n}$ and $\tau_{2,n}$ associated to them [23]. One can then express [24] the non-equilibrium part of the NMR signal collected in the inversion-recovery, for T_1 measurements, or CPMG, for T_2 measurements, experiments as

$$M_\alpha(t) = m_0 \sum_n \langle 1|\Psi_{\alpha,n}\rangle^2 \exp(-t/\tau_{\alpha,n}) \tag{3}$$

and conclude that corresponding 1D spectra, obtained after the ILT, has non-zero values only for the times $\tau_{\alpha,n}$ with positive intensities

$$S_{T_\alpha}(n) = m_0 \sum_n \langle 1|\Psi_{\alpha,n}\rangle^2 \tag{4}$$

where m_0 is the magnetisation density at equilibrium and $|1\rangle$ stands for a homogeneous magnetisation state equal to one all over the system. Using the same eigen-states, the intensities of the T_1–T_2 and T_2–T_2 correlation spectra for coordinates $(\tau_{1,n}, \tau_{2,m})$ and $(\tau_{2,n}, \tau_{2,m})$ were analytically calculated [22] as

$$S_{T_1-T_2}(n, m) = m_0 \langle 1|\Psi_{1,n}\rangle\langle\Psi_{1,n}|\Psi_{2,m}\rangle\langle\Psi_{2,m}|1\rangle \tag{5}$$

$$S_{T_2-T_2}(n, m) = m_0 \sum_p \langle 1|\Psi_{2,n}\rangle\langle\Psi_{2,n}|\Psi_{1,p}\rangle\langle\Psi_{1,p}|\Psi_{2,m}\rangle\langle\Psi_{2,m}|1\rangle$$
$$\times \exp(-\tau_{mix}/\tau_{1,p}) \tag{6}$$

where τ_{mix} is the duration of the mixing period. From physical point of view, the peaks observed in the spectra indicate a correlation or exchange between various relaxation modes. We could obtain the amplitudes of the peaks in the T_1–T_1 spectrum by exchanging indices 1 and 2 in Eq. (6).

3. Previous structural results

From Eqs. (5) and (6), the authors of [22] made appear the following important properties, though, largely ignored in numerous recent experimental studies, and which deserves that we give them special emphasis

(**a**) The T_2–T_2 spectra are symmetrical according to $S_{T_2-T_2}(n, m) = S_{T_2-T_2}(m, n)$.

(**b**) When eigen-modes $|\Psi_{1,n}(\mathbf{r})\rangle$ and $|\Psi_{2,n}(\mathbf{r})\rangle$ are identical, the T_1–T_2 and T_2–T_2 spectra have diagonal peaks only.

(**c**) The spectra can contain peaks with negative amplitudes, as was showed theoretically for 1D pores. Quite clearly, the ILT algorithm available to the NMR spectroscopists at the moment does not allow observation of such peaks experimentally. We shall attach particular attention to whether these negative peaks are merely occasional minor faults, which can be ignored, or systematically encountered major features of the relaxation correlation spectra, to take into account in analysis.

4. Results and discussion

Unfortunately, the above-mentioned expressions have not, we believe, been exploited enough and we now show that they can indeed provide much more information on general features of the spectra. For the sake of simplicity, we shall limit ourselves in what follows to the case of non-degenerated relaxation states knowing that the results obtained below can be easily extended to the more general case. Taking into account formal similarity between the T_1–T_1 and T_2–T_2 spectra, we shall hereafter discuss the T_1–T_2 and T_2–T_2 spectra only.

(**d**) The sum of the intensities of all peaks in the spectrum is preserved, i.e. independent of the durations of the relaxation periods. This conservation law is deduced from the closure relation

$$\sum_n |\Psi_{\alpha,n}\rangle\langle\Psi_{\alpha,n}| = Id \tag{7}$$

by writing

$$\sum_{n,m} S_{T_1-T_2}(n, m) = m_0\langle 1|1\rangle = M_1(0) \tag{8}$$

and

$$\sum_{n,m} S_{T_2-T_1}(n,m) = m_0 \sum_n \langle 1|\Psi_{1,n}\rangle^2 \exp(-\tau_{mix}/\tau_{1,n})$$

$$= M_1(\tau_{mix}) \qquad (9)$$

and noting that $\langle 1|1\rangle$ is the volume of the fluid. Thus the overall intensity of the T_1–T_2 spectra is equal to the total magnetisation of the system at equilibrium and that of the T_2–T_2 spectra is equal to the magnetisation that would remain, had the system been subject to spin–lattice relaxation during the mixing period T_{mix} only.

(**e**) The projection of the T_1–T_2 spectrum on to one of the coordinate axes is equal to the corresponding 1D spectrum:

$$\sum_n S_{T_1-T_2}(n,m) = m_0 \langle 1|\Psi_{2,m}\rangle^2 = S_{T_2}(m) \qquad (10)$$

and

$$\sum_m S_{T_1-T_2}(n-m) = m_0 \langle 1|\Psi_{1,n}\rangle^2 = S_{T_1}(n) \qquad (11)$$

(**f**) A spin–lattice relaxation eigen-mode that gives rise to no peak in the 1D spectrum will produce neither diagonal nor cross-peaks in the 2D T_1–T_2 and T_1–T_1 spectra. Alike a spin–spin relaxation eigen-mode that gives rise to no peak in the 1D spectrum will produce neither diagonal nor cross-peaks in the 2D T_1–T_2 and T_2–T_2 spectra. This can be inferred, e.g., by noting that

$$S_{T_1-T_2}(m,n') = S_{T_2-T_2}(m,n') = S_{T_2-T_2}(n',m) = 0 \qquad (12)$$

for any m, when for a certain mode $|\Psi_{2,n'}\rangle$ the intensity $S_{T_2}(n') = 0$ and so $\langle 1|\Psi_{2,n'}\rangle = 0$.

(**g**) All diagonal peaks in the T_1–T_1 and T_2–T_2 spectra have positive amplitudes, as they can be expressed as a sum of only positive terms, e.g.

$$S_{T_2-T_2} = m_0 \sum_p \langle 1|\Psi_{2,n}\rangle^2 \langle \Psi_{2,n}|\Psi_{1,p}\rangle^2 \exp(-\tau_{mix}/\tau_{1,p}) \qquad (13)$$

(**h**) Unless the spin–lattice and spin–spin relaxation modes are identical, there will be always peaks with negative amplitude in the T_1–T_2 spectra. To see this, we note that it is always possible to choose bases $|\Psi_{1,n}\rangle$ and $|\Psi_{2,n}\rangle$ for which $\langle 1|\Psi_{1,n}\rangle \geq 0$ and $\langle 1|\Psi_{2,n}\rangle \geq 0$. Most often these inequalities are strict. Moreover, the scalar products $u_{n,m} = \langle \Psi_{1,n}|\Psi_{2,m}\rangle$ are the coefficients of the unitary matrix $U = (u_{n,m})$ that gives the expressions of modes $|\Psi_{1,n}\rangle$ in the base of the modes $|\Psi_{2,n}\rangle$. This matrix satisfies the fundamental property $U^t U = Id$. When the two sets of modes are different, U can not be diagonalised by simply swapping its lines and columns, and has necessarily negative coefficients, i.e. there exist numerous indices (n',m') for which $\langle \Psi_{1,n'} | \Psi_{2,m'}\rangle < 0$. The intensity of the corresponding cross-peak will be negative:

$$S_{T_1-T_2}(n',m') = m_0 \langle 1|\Psi_{1,n'}\rangle \langle \Psi_{1,n'}|\Psi_{2,m'}\rangle \langle \Psi_{2,m'}|1\rangle \leq 0 \qquad (14)$$

where equality takes place when $\langle 1|\Psi_{1,n}'\rangle = 0$ or $\langle 1|\Psi_{2,m'}\rangle = 0$ only. This would happen, should $|1\rangle$ itself be a relaxation mode $|\Psi_{\alpha,n}\rangle$ which case it would be orthogonal to all other modes $|\Psi_{\alpha,n}\rangle$. This situation is, though, of no practical interest, as then only one mode is observable. Another situation where there may be numerous modes orthogonal to $|1\rangle$ is that of a system with a symmetry that relates two families of relaxation modes, i.e. symmetrical and so 'observable' modes, on the one hand, and anti-symmetrical unobservable modes, on the other hand. It is then possible to apply the arguments developed above to the subspace of symmetrical modes only and infer that such system will also necessarily give rise to negative peaks. Negative peaks in a few particular systems have already been reported in preceding theoretical studies

[21,22]. Our study shows that their presence in spectra is far from being accidental: they constitute a rather major feature of the spectra, whose experimentally observation has been hindered by the lack of a more adequate ILT algorithm.

(**i**) If there is a non-diagonal peak (n, m) in a T_1–T_1 or T_2–T_2 spectrum, there exists at least one index p for which $\langle 1|\Psi_{2,n}\rangle \langle \Psi_{2,n}|\Psi_{1,p}\rangle \neq 0$ and $\langle \Psi_{1,p}|\Psi_{2,m}\rangle \langle \Psi_{2,m}|1\rangle \neq 0$ and so the spectrum will also contain the diagonal peaks (n, n) and (m, m).

(**j**) If two diagonal peaks (n, n) and (m, m) give rise to a pair of cross-peaks (n, m) and (m, n), the sum of the absolute values of the intensities of the latter will never exceed that of the former. This can be seen by setting $a = \langle 1|\Psi_{2,n}\rangle \langle \Psi_{2,n}|\Psi_{1,p}\rangle$ and $b = \langle \Psi_{1,p}|\Psi_{2,m}\rangle \langle \Psi_{2,m}|1\rangle$ in the relation $|ab| \leq (a^2 + b^2)/2$ to deduce

$$|S_{T_2-T_2}(n,m)| \leq (S_{T_2-T_2}(n,n) + S_{T_2-T_2}(m,m))/2 \qquad (15)$$

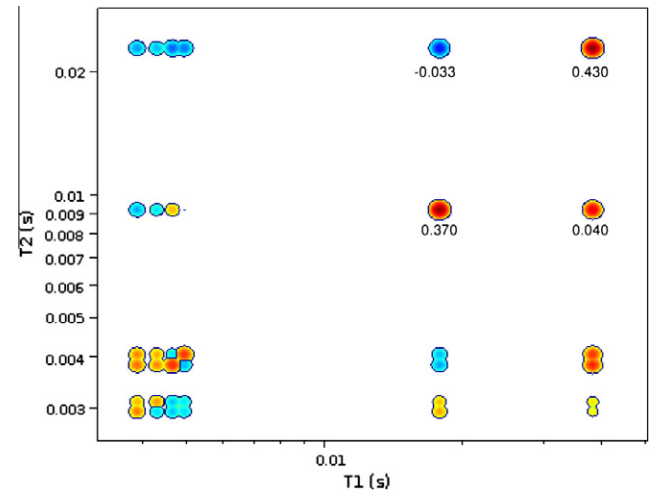The experimental data reported so far corroborates the statement [18,21].

Fig. 1. The computer-simulated T_1–T_2 spectrum of the model porous system of Fig. 3 The positive and negative peaks are coloured in red/yellow and blue respectively. The normalised amplitude of some peaks is indicated. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
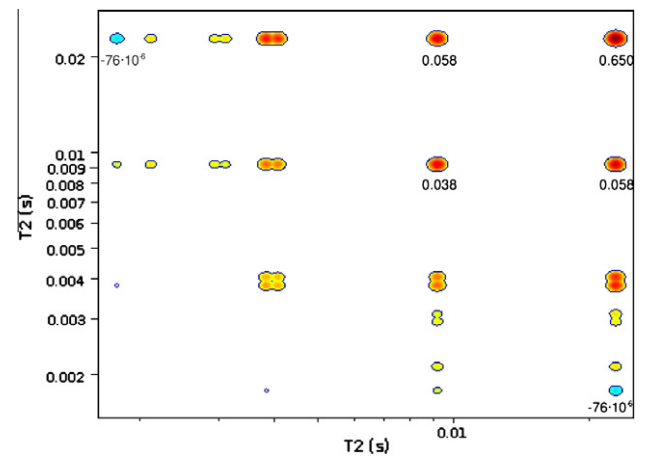

Fig. 2. The computer-simulated T_2–T_2 spectrum of the model porous system of Fig. 3 The positive and negative peaks are coloured in red/yellow and blue respectively. The normalised amplitude of some peaks is indicated. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)
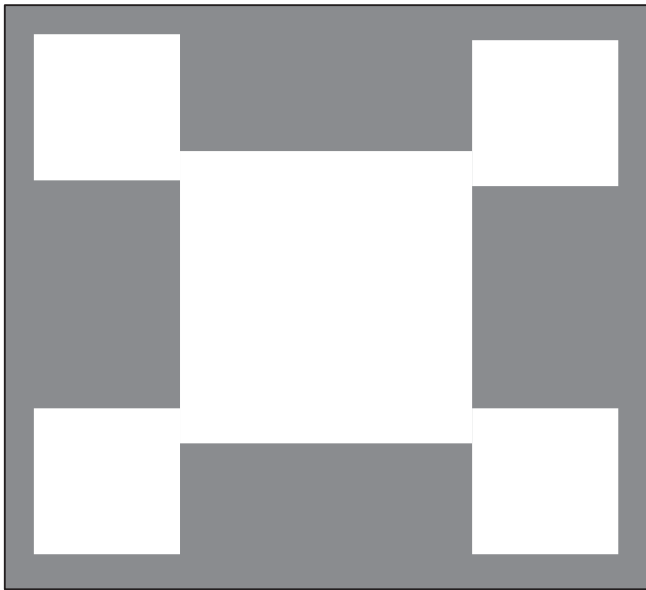
Fig. 3. Model porous system for which the spectra of Figs. 1 and 2 were simulated. The inside of the pores is in white and the solid matrix is coloured in grey. The dimensions of the system are 10 by 10 μm. Diffusion was assumed to be uniform and isotropic: the diffusion coefficient was set to 10^{-10} m^2/s. The surface relaxation rates for calculation of the spin–lattice and spin–spin relaxation eigne-modes were set to 4×10^{-5} and 10^{-4} m/s respectively. Both spin–lattice and spin–spin bulk relaxation time inside the pores was set to 0.1 s.

5. Experimental

Figs. 1 and 2 show, respectively, the T_1–T_2 and T_2–T_2 spectra we simulated for the 2D model porous system of Fig. 3. We computed fifty eigen-modes and values using the finite difference approach [25], and we introduced them into Eqs. (5) and (6) to calculate the spectra. We coded our algorithm in Fortran 95 programming language. The spectra feature several of the structural properties established above. The diagonal peaks in the T_2–T_2 spectrum have positive amplitude, as could be expected from (g). The T_2–T_2 spectrum is symmetric with respect to its diagonal, as had been predicted in (a). Most importantly, both T_1–T_2 and T_2–T_2 spectra contain negative components. A detailed description of simulation of the 2D relaxation spectra and discussion of their properties will be the subject of a separate manuscript.

6. Conclusions

We demonstrated how useful the eigen-modes formalism can be in elucidating fundamental properties of 2D ILT spectra of diffusive systems. Several of such properties were thus discovered. Knowing these properties can help to identify flaws in design of NMR experimental schemes and to anticipate defects that can be introduced by the presently available ILT algorithm in such spectra. Specifically, we pointed out that there is a limit to the cross-peak intensities that can be achieved experimentally. Finally, the most striking inference we could draw is that the negative components, previously noticed in a few theoretical studies, are an intrinsic feature of all T_1–T_2 spectra, thus underlining a great necessity to pursue efforts in developing more adequate algorithms for ILT.

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