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A system theoretic formulation of NMR experiments

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A detailed system theoretic description is given of NMR experiments including relaxation effects. The approach is based on an exact and analytical solution to the master equation. It is shown that NMR experiments can be described in the framework of bilinear time-invariant systems. This description is used to derive closed-form expressions for the spectrum of one- and two-dimensional experiments. The simulations show that the approach accounts for the frequency dependence of a pulse, distinguishes between soft and hard pulses and also explains artifacts such as axial peaks.

1. Introduction

In this paper we present a formulation of NMR experiments in the language of systems theory. Systems theory has played a major role in such areas as control theory, econometrics and signal processing (see e.g. [1–3]). In particular, state space methods have proven to be very suitable tools for the modelling and analysis of a large array of applications. One of the main reasons for the success of these methods is that using state space theory many problems can be translated to equivalent problems in linear algebra and can therefore be analyzed using the powerful theoretical and numerical methods that are available in linear algebra.

Whilst system theoretic ideas have also played a role before in NMR, (see e.g. [4]), most of the influence that systems theory had on NMR has been through the input-output formulation. However, the authors of this paper are not aware of a systematic discussion of state-space methods applied to NMR problems, especially for 2-D experiments. In [5,6] some state space methods are used to analyze 1-D NMR experiments from a statistical point of view. With the results that are presented in this paper we hope to be able to provide the basis for the application of system theoretic methods to the design and analysis of NMR experiments.

A general description of NMR experiments is presented in the following section

where it is shown that the dynamics of an NMR experiment can be represented by a bilinear system. The method which is used to reformulate the master equation as a bilinear system is the well-established technique of the translation of the density matrix formulation to the language using superoperators in Liouville space (see e.g. [4]). An important point is, however, that the state of the bilinear system at a particular time is given by the difference of the density matrix at this time and the equilibrium density matrix. Use of this setup allows us to incorporate relaxation into the description and allows for the use of stability results to analyze NMR experiments. It should, however, be stressed that our description using the framework of bilinear systems is mathematically equivalent to the framework which uses the master equation as it is usually used in the analysis of NMR experiments.

In the following section we discuss the solution of the bilinear system given a constant input. The solution that we present is exact and given through basic functions of the system matrices. In this way we use an approach which is different from approaches which use approximate solutions to the master equation, such as those which are based, for example, on the product operator formulism. Of course, due to the above mentioned equivalence of the bilinear system with the master equation, the exact solution that we use is equivalent to an exact solution of the master equation.

Next we introduce a general description of 2-D experiments. We obtain a closed form representation of the spectrum of a 2-D experiment using the matrices that characterize the spin system and the particular experiment. We also discuss approximations such as the *pulse approximation* and the *low-relaxation approximation*. Using these approximations, simplifications for the expressions of the spectrum can be obtained. In our description none of the otherwise standard assumptions have to be made such as the high-temperature approximation.

In the final section standard experiments are discussed within our framework. We consider a 1-D basic pulse experiment, 2-D J-spectroscopy and a COSY experiment. The experiments are chosen to serve as basic examples for the techniques that are developed in this paper. In the 1-D experiment, the simulated spectrum shows the loss of power of the 90 degree pulse away from resonance. The examples were coded in MatLab and only a few lines of code were necessary to produce the simulations.

In this paper we will make repeated use of basic identities on the Kronecker product $\otimes$ and the *vec* operation (see e.g. [7]). The *vec* operation takes a matrix A and produces a vector by stacking the columns of A below one another. We denote by A^T the transpose of the matrix A and by A^* the adjoint of the matrix, i.e. A^* is the transpose together with a complex conjugation of the matrix entries.

2. Basic setup

In this section we present an abstract approach to the basic formulation of

NMR experiments. Starting with the master equation we derive what we call the master system in error vector representation, which is a bilinear system. We then discuss general state space transformations, which are equivalent to changing the coordinate system from the laboratory frame to the rotating frame. The role which stability plays in the context of relaxation is then pointed out. Stability of the spin system, while being a natural concept, is also an important technical property for the subsequent analysis of pulse experiments. Given this abstract framework it is then quite straightforward to write down a closed form representation of the Fourier transform of a 1-D experiment.

In defining the framework within which we are working we start with the master equation (see e.g. [4]) and combine with it the measurement equation, i.e. we assume that the dynamics of a spin system are described by the so-called *master system*:

$$\dot{\sigma}(t) = -i[H(t), \sigma(t)] - \hat{R}[\sigma(t) - \sigma_{eq}], \quad \sigma(t_0) = \sigma_0,$$

$$y(t) = trace(M\sigma(t)), \quad t \geqslant t_0.$$

Here $\sigma(t)$ is a $n \times n$ matrix-valued function. The $n \times n$ matrix-valued function $H(t)$, $t \geqslant t_0$ is the *Hamiltonian* of the system. The $n \times n$ matrix σ_{eq} is the equilibrium density matrix. The symbol $\hat{R}$ stands for the *relaxation super operator*. The $n \times n$ matrix M is called the *measurement matrix*. The first equation is the well-known *master equation*. The second equation is called the *measurement equation*. The function y is the function of measured values, i.e. the signal given by the induced magnetization.

ASSUMPTIONS

Throughout the paper we will make the following assumptions.

- **A1**: The Hamiltonian $H(t)$ is a $n \times n$ hermitian matrix-valued function which can be decomposed into two hermitian parts H_1 and H_2, i.e. $H(t) = H_1 + H_2(t)$, $t \geqslant t_0$, where H_1 is a constant matrix and $H_2(t) = \sum_{j=1}^{k} u_j(t) H_{2,j}$, with $H_{2,j}$ a constant hermitian matrix, and u_j a scalar real-valued function, $j = 1, 2, \ldots, k$. Then the master system can be written as

$$\dot{\sigma}(t) = -i[H_1, \sigma(t)] - i\sum_{j=1}^{k} u_j(t)[H_{2,j}, \sigma(t)] - \hat{R}[\sigma(t) - \sigma_{eq}], \quad \sigma(t_0) = \sigma_0,$$

$$y(t) = trace(M\sigma(t)), \quad t \geqslant t_0.$$

- **A2**: The $n \times n$ equilibrium matrix σ_{eq} is hermitian and commutes with H_1, i.e. $[H_1, \sigma_{eq}] = 0$.

- **A3**: If R is the matrix representation of $\hat{R}$, i.e. $Rvec(\sigma) = vec(\hat{R}(\sigma))$ for each $n \times n$ matrix σ, then we assume that R is hermitian.

For our purposes it is often more convenient to rewrite the master system as a system whose underlying differential equation is a vector differential equation, rather than a matrix differential equation. This transition is simply a rewriting of the basic equations in the language of superoperators. To this effect we define

$$v(t) := vec(\sigma(t)), \quad t \geqslant t_0,$$

$$v_{eq} := vec(\sigma_{eq}),$$

$$A_v := -i(I \otimes H_1 - H_1^T \otimes I),$$

$$N_j := -i(I \otimes H_{2j} - H_{2j}^T \otimes I), \quad j = 1, \ldots, k,$$

$$c := (vec(M^T))^T,$$

(the identity matrix I has the same dimensions as the matrices H_1 and H_{2j}, $j = 1, \ldots, k$), and let R be the matrix representation of the super operator $\hat{R}$. By simple application of results on Kronecker products and the *vec* operation we have that the master system is equivalent to

$$\dot{v}(t) = A_v v(t) + \left(\sum_{j=1}^{k} u_j(t) N_j\right) v(t) - R(v(t) - v_{eq}), \quad v(t_0) = v_0,$$

$$y(t) = cv(t), \quad t \geqslant t_0.$$

This system is called the *master system in vector representation*. A further equivalent representation of the master system is obtained if we consider the error function e between v and v_{eq}, i.e. for $t \geqslant t_0$

$$e(t) := v(t) - v_{eq}.$$

Using the assumption that $[H_1, \sigma_{eq}] = 0$, which is equivalent to $A_v v_{eq} = 0$, we obtain

$$\dot{e}(t) = Ae(t) + \left(\sum_{j=1}^{k} u_j(t) N_j\right) e(t) + \sum_{j=1}^{k} b_j u_j(t), \quad e(t_0) = e_0,$$

$$y(t) = ce(t) + c_0, \quad t \geqslant t_0,$$

where $A := A_v - R$, $b_j := N_j v_{eq}$, $j = 1, \ldots, k$, $e_0 = v(0) - v_{eq}$ and $c_0 = cv_{eq}$. This system is called the *master system in error vector representation*. Note that if $c_0 = 0$, this system is a standard continuous-time bilinear state space system (see e.g. [8]). We will therefore also refer to e as the *state* of the system, $u_1, \ldots, u_k$ as the *inputs* of the system and y as its *output*. Note that $c_0 = 0$ is equivalent to the equilibrium state of the system not generating an observable signal, which is the case in all standard experimental setups. From now on we therefore make the assumption

- **A4**: $c_0 = cv_{eq} = 0$.

In the following proposition it is shown that a suitable coordinate transformation can simplify the bilinear equation. This operation is simply a generalization of the standard transformation of the laboratory frame to the rotating frame.

PROPOSITION 1

Let

$$\dot{e}(t) = Ae(t) + \left(\sum_{j=1}^{k} u_j(t) N_j\right) e(t) + \sum_{j=1}^{k} b_j u_j(t), \quad e(t_0) = e_0,$$

$$y(t) = ce(t), \quad t \geqslant t_0,$$

be a master system in error vector representation, with the above assumptions and notation. Let $T(t) := e^{F(t-t_0)}$, $t \geqslant t_0$, for some $n \times n$ matrix F and set $x(t) := T(t)e(t)$, $t \geqslant t_0$. If $T(t)AT^{-1}(t) = A$, for $t \geqslant t_0$, then the master system in error vector representation is equivalent to the following system with state vector x:

$$\dot{x}(t) = (A + F)x(t) + \sum_{j=1}^{k} u_j(t) T(t) N_j T^{-1}(t) x(t) + \sum_{j=1}^{k} T(t) b_j u_j(t),$$

$$x(t_0) := x_0 := e_0,$$

$$y(t) = cT^{-1}(t)x(t), \quad t \geqslant t_0.$$

Proof

Note that $\dot{T}(t) = FT(t)$, $t \geqslant t_0$. Since $x(t) = T(t)e(t)$, it follows that $\dot{x}(t) = \dot{T}(t)e(t) + T(t)\dot{e}(t) = Fx(t) + T(t)\dot{e}(t)$, $t \geqslant t_0$. Therefore,

$$\dot{x}(t) = Fx(t) + T(t)\dot{e}(t) = Fx(t) + T(t)\left[Ae(t) + \sum_{j=1}^{k} u_j(t) N_j e(t) + \sum_{j=1}^{k} b_j u_j(t)\right]$$

$$= Fx(t) + T(t)AT^{-1}(t)T(t)e(t) + \sum_{j=1}^{k} u_j(t) T(t) N_j T^{-1}(t) T(t) e(t)$$

$$+\sum_{j=1}^{k} T(t)b_j u_j(t)$$

$$= (A+F)x(t) + \sum_{j=1}^{k} u_j(t)T(t)N_j T^{-1}(t)x(t) + \sum_{j=1}^{k} T(t)b_j u_j(t), \quad t \geqslant t_0,$$

with $x(t_0) = T(t_0)e(t_0) = e(t_0) = e_0$ and

$$y(t) = ce(t) = cT^{-1}(t)T(t)e(t) = cT^{-1}(t)x(t), \quad t \geqslant t_0. \qquad \square$$

As is stands, this result is not very useful. But in a concrete situation it will turn out that, as would of course be expected from the very standard results on changing the coordinate system, for specifically chosen inputs and matrix F, the terms $\sum_{j=1}^{k} u_j(t)T(t)N_j T^{-1}(t)$ and $\sum_{j=1}^{k} T(t)b_j u_j(t)$ are time invariant.

The stability of the master system in error vector representation will be an important technical tool in later sections. A condition for the stability of the system is given in the following Proposition. The system is called stable if for each e_0, $e^{tA}e_0 \to 0$ as $t \to \infty$. The system is therefore stable if in the absence of any input, the state vector decays to zero. This means that the system approaches equilibrium as $t \to \infty$.

PROPOSITION 2

Assume that A_v commutes with R. Then the system is stable if all eigenvalues of R are in the open right half plane.

Proof

This follows from standard stability results (see e.g. [9]). $\square$

If we assume that the system is in state e_0 at time 0 and no input is applied for $t \geqslant 0$ the measured signal is given by

$$y(t) = ce^{tA}e_0, \quad t \geqslant 0.$$

If the system is stable we can apply the Fourier transform and we obtain for $\omega \in \mathfrak{R}$,

$$\mathcal{F}(y)(\omega) = \int_0^\infty ce^{tA}e_0 e^{-i\omega t}dt = c\left(\int_0^\infty e^{t(A-i\omega I)}dt\right)e_0$$

$$= c((A - i\omega I)^{-1})e^{t(A-i\omega I)}\,|_0^\infty)e_0 = c(i\omega I - A)^{-1}e_0.$$

3. Inputs and pulses

We now present an abstract solution to the master system in error vector representation given a constant input. The importance of this result is that the solution is given in terms of the underlying system matrices and can therefore be easily computed using a numerical linear algebra package such as MatLab.

The relevance of analyzing the system given a constant input is that in a suitable rotating frame (Proposition 1) the system with certain sinusoidal inputs is constant.

PROPOSITION 3

Let

$$\dot{x}(t) = Ax(t) + \left(\sum_{j=1}^{k} N_j u_t(t)\right)x(t) + \sum_{j=1}^{k} b_j u_j(t), \quad x(t_0) = x_0,$$

$$y(t) = cx(t)$$

be the master system in error vector representation. Let the inputs to the system be given by

$$u_j(t) = \begin{cases} u_j^0, & t_0 \leqslant t \leqslant T, \\ 0, & t > T, \end{cases}$$

where $u_j^0 \in \mathfrak{R}$. Assume that $A_p := A + \sum_{j=1}^{k} u_j^0 N_j$ is invertible, then

$$x(t) = \begin{cases} [e^{(t-t_0)A_p} - I]A_p^{-1} b_p + e^{(t-t_0)A_p} x_0, & t_0 \leqslant t \leqslant T, \\ e^{(t-T)A}([e^{(T-t_0)A_p} - I]A_p^{-1} b_p + e^{(T-t_0)A_p} x_0), & t > T, \end{cases}$$

where $b_p = \sum_{j=1}^{k} b_j u_j^0$.

Proof

Note that for $t_0 \leqslant t \leqslant T$ we have

$$\dot{x}(t) = Ax(t) + \left(\sum_{j=1}^{k} u_j^0 N_j\right)x(t) + \sum_{j=1}^{k} b_j u_j^0 = A_p x(t) + b_p.$$

Hence

$$x(t) = \int_{t_0}^{t} e^{(t-s)A_p} b_p \, ds + e^{(t-t_0)A_p} x_0.$$

Since A_p is invertible we therefore have

$$x(t) = (e^{tA_p}(-A_p^{-1})[e^{-sA_p}\,|_{t_0}^{t}])b_p + e^{(t-t_0)A_p}x_0$$

$$= [e^{(t-t_0)A_p} - I]A_p^{-1}b_p + e^{(t-t_0)A_p}x_0\,.$$

The expression for $t > T$ follows immediately from here. □

Note that a similar expression was derived in [6]. In NMR calculations often the approximation

$$A_p \equiv \sum_{j=1}^{k} u_j^0 N_j$$

is used (see e.g. [4,10]) while a pulse is applied. We call this approximation the *pulse approximation*. Given the pulse approximation the solution in the previous proposition is simplified.

PROPOSITION 4

Let the notation and assumptions be given as in the previous proposition. Moreover, assume the pulse approximation and that $b_j = N_j v_{eq}$, $j = 1, \ldots, k$, for some vector v_{eq}. Then

$$x(t) = \begin{cases} (e^{(t-t_0)(\sum_{j=1}^{k} u_j^0 N_j)} - I)v_{eq} + e^{(t-t_0)(\sum_{j=1}^{k} u_j^0 N_j)}x_0\,, & t_0 \leqslant t \leqslant T\,, \\ e^{(t-T)A}\left((e^{(T-t_0)(\sum_{j=1}^{k} u_j^0 N_j)} - I)v_{eq} + e^{(T-t_0)(\sum_{j=1}^{k} u_j^0 N_j)}x_0,\right), & t > T\,, \end{cases}$$

$$= \begin{cases} e^{(t-t_0)(\sum_{j=1}^{k} u_j^0 N_j)}(v_{eq} + x_0) - v_{eq}\,, & t_0 \leqslant t \leqslant T\,, \\ e^{(t-T)A}\left(e^{(T-t_0)(\sum_{j=1}^{k} u_j^0 N_j)}(v_{eq} + x_0) - v_{eq}\right), & t > T\,. \end{cases}$$

Proof

The proof follows by verification. □

4. Two-dimensional experiments

Using the general setup introduced in the previous sections we can now analyze two dimensional pulse experiments. In this section we will present a general theory of these experiments from our point of view. The aim is to derive a general representation of the spectrum of a 2-D experiment in terms of the underlying system matrices.

We assume that the spin dynamics are governed by the master system in error vector representation,

$$\dot{e}(t) = Ae(t) + \left(\sum_{j=1}^{k} u_j(t)N_j\right)e(t) + \sum_{j=1}^{k} b_j u_j(t)\,, \quad e(t_0) = e_0\,,$$

$$y(t) = ce(t)\,, \quad t \geqslant t_0\,.$$

We define a family of input vector functions $((u^{t_1})_{t_1 \geqslant 0})$ in the following way. For each $t_1 \geqslant 0$ let f_i, $i = 1, 2, 3$, be an input defined on a time interval Δ_i, $i = 1, 2, 3$, such that if the system is in state e_1 at the beginning of the interval Δ_i, $i = 1, 2, 3$, then the system will be in state

$$e_2 = T_i e_1 + e_i^0\,, \quad i = 1, 2, 3\,,$$

at the end of the interval where T_i, is a constant matrix, and e_i^0 is a constant vector, $i = 1, 2, 3$. That this representation is justified follows from Proposition 3 and Proposition 4 since a combination of pulses and evolution periods leads to such an affine transformation of the state of the system.

For $t_1 \geqslant 0$ the input u^{t_1} is then defined by

$$u^{t_1} = \begin{cases} f_1, & 0 \leqslant t \leqslant \Delta_1\,, \\ 0, & \Delta_1 < t \leqslant \Delta_1 + k_1 t_1\,, \\ f_2, & \Delta_1 + k_1 t_1 < t \leqslant \Delta_1 + \Delta_2 + k_1 t_1\,, \\ 0, & \Delta_1 + \Delta_2 + k_1 t_1 < t \leqslant \Delta_1 + \Delta_2 + t_1\,, \\ f_3, & \Delta_1 + \Delta_2 + t_1 < t \leqslant \Delta_1 + \Delta_2 + \Delta_3 + t_1\,, \\ 0, & t \geqslant \Delta_1 + \Delta_2 + \Delta_3 + t_1\,, \end{cases}$$

where $0 \leqslant k_1 \leqslant 1$ is fixed and determined by the particular experiment. If $k_1 = 0$ or $k_1 = 1$ then the obvious simplifications can be given. For each input u^{t_1}, $t_1 \geqslant 0$, the output y of the system is measured for $t \geqslant \Delta_1 + \Delta_2 + \Delta_3 + t_1$ and set for $t_2 \geqslant 0$

$$s(t_1, t_2) := y(\Delta_1 + \Delta_2 + \Delta_3 + t_1 + t_2) = cx(\Delta_1 + \Delta_2 + \Delta_3 + t_1 + t_2)\,.$$

For each $t_1 \geqslant 0$ the state x_{t_1} of the system at time $\Delta_1 + \Delta_2 + \Delta_3 + t_1$ is given by

$$x_{t_1} = T_3 e^{k_2 t_1 A}(T_2 e^{k_1 t_1 A}(T_1 x_0 + e_1^0) + e_2^0) + e_3^0$$

and

$$x(\Delta_1 + \Delta_2 + \Delta_3 + t_1 + t_2) = e^{t_2 A} x_{t_1}$$
$$= e^{t_2 A}(T_3 e^{k_2 t_1 A}(T_2 e^{k_1 t_1 A}(T_1 x_0 + e_1^0) + e_2^0) + e_3^0)$$
$$= e^{t_2 A} T_3 e^{k_2 t_1 A} T_2 e^{k_1 t_1 A} T_1 x_0 + e^{t_2 A} T_3 e^{k_2 t_1 A} T_2 e^{k_1 t_1 A} e_1^0$$
$$+ e^{t_2 A} T_3 e^{k_2 t_1 A} e_2^0 + e^{t_2 A} e_3^0 .$$

Therefore

$$s(t_1, t_2) = c e^{t_2 A}(T_3 e^{k_2 t_1 A}(T_2 e^{k_1 t_1 A}(T_1 x_0 + e_1^0) + e_2^0) + e_3^0)$$
$$= c e^{t_2 A} T_3 e^{k_2 t_1 A} T_2 e^{k_1 t_1 A} T_1 x_0 + c e^{t_2 A} T_3 e^{k_2 t_1 A} T_2 e^{k_1 t_1 A} e_1^0$$
$$+ c e^{t_2 A} T_3 e^{k_2 t_1 A} e_2^0 + c e^{t_2 A} e_3^0 .$$

We would now like to calculate the two dimensional Fourier transform of s,

$$G(\omega_1, \omega_2) = \int_0^\infty \int_0^\infty s(t_1, t_2) e^{-i t_1 \omega_1} e^{-i t_2 \omega_2} dt_1 dt_2$$
$$= c(i\omega_2 I - A)^{-1}[T_3 P(\omega_1)(T_1 x_0 + e_1^0)$$
$$+ T_3(i\omega_1 I - k_2 A)^{-1} e_2^0 + \delta_0(\omega_1) e_3^0] ,$$

where $P(\omega_1) := \int_0^\infty e^{k_2 t_1 A} T_2 e^{k_1 t_1 A} e^{-i\omega_1 t_1} dt_1$ and $\delta_0(\omega_1)$ stands for the delta function with mass concentrated at 0. If $x_0 = 0$, which is the case if the experiment is started at equilibrium, then

$$G(\omega_1, \omega_2) = c(i\omega_2 I - A)^{-1}[T_3 P(\omega_1) e_1^0 + T_3(i\omega_1 I - k_2 A)^{-1} e_2^0 + \delta_0(\omega_1) e_3^0] .$$

If no pulse is applied during the evolution period, i.e. if $T_2 = I$ and $e_2^0 = 0$, then

$$G(\omega_1, \omega_2) = c(i\omega_2 I - A)^{-1}[T_3(i\omega_1 I - A)^{-1}(T_1 x_0 + e_1^0) + \delta_0(\omega_1) e_3^0] .$$

Moreover, if $x_0 = 0$, then

$$G(\omega_1, \omega_2) = c(i\omega_2 I - A)^{-1}[T_3(i\omega_1 I - A)^{-1} e_1^0 + \delta_0(\omega_1) e_3^0] .$$

If on the other hand there is no third pulse, then $T_3 = I$ and $e_3^0 = 0$, therefore

$$G(\omega_1, \omega_2) = c(i\omega_2 I - A)^{-1}[P(\omega_1)(T_1 x_0 + e_1^0) + (i\omega_1 I - k_2 A)^{-1} e_2^0] .$$

Moreover, if $x_0 = 0$ then

$$G(\omega_1, \omega_2) = c(i\omega_2 I - A)^{-1}[P(\omega_1) e_1^0 + (i\omega_1 I - k_2 A)^{-1} e_2^0] .$$

In the following lemma a result is given which shows that $P(\omega_1)$ can be computed using only linear algebra operations. Therefore $G(\omega_1, \omega_2)$ can be calculated by only using matrix computations.

LEMMA 1

Let A be a $n \times n$ matrix such that the eigenvalues of A are all in the open left half plane. Then for $k_1, k_2 \geqslant 0$ such that $k_1 + k_2 = 1$ and T an $n \times n$ matrix, the integral

$$P(\omega) := \int_0^\infty e^{tk_2A} T e^{tk_1A} e^{-it\omega} dt$$

exists and

$$vec(P(\omega)) = [i\omega I - (I \otimes (k_2A) + (k_1A^T) \otimes I)]^{-1} vec(T) .$$

If $T = I$, then $P(\omega) = (i\omega I - A)^{-1}, \omega \in \Re$.

Proof

Note that since the eigenvalues of A are in the open left half plane the integral $P(\omega)$ exists for all $\omega \in \Re$. By a standard result ([11]) on Lyapunov equations $P(\omega)$ is the unique solution to the Lyapunov equation

$$(k_2A - i\omega I)P(\omega) + P(\omega)(k_1A) = -T .$$

The solution X to the matrix equation

$$AX + XB = C$$

can be written as [7,11]

$$vec(X) = (I \otimes A + B^T \otimes I)^{-1} vec(C) .$$

Hence

$$\begin{aligned} vec(P(\omega)) &= [I \otimes (k_2A - i\omega I) + (k_1A^T) \otimes I]^{-1} vec(-T) \\ &= [i\omega I - (I \otimes (k_2A) + (k_1A^T) \otimes I)]^{-1} vec(T) . \end{aligned}$$

The case for $T = I$ is obvious. □

If we assume the pulse approximation and also assume that during periods Δ_1, Δ_2, Δ_3 only pulses are applied and no evolution takes place, then we obtain

$$\begin{aligned} s(t_1, t_2) = ce^{t_2A}\big(T_3\big(e^{k_2t_1A} T_2(e^{k_1t_1A} T_1\big(x_0 + v_{eq}\big) \\ - e^{k_1t_1A} v_{eq} + v_{eq}) - e^{k_2t_1A} v_{eq} + v_{eq}\big) - v_{eq}\big) , \end{aligned}$$

$t_1, t_2 \geqslant 0$. This expression will be more compact if we also assume the *low-relaxation approximation* (*in the evolution period*), by which we assume that in the above expression

$$-e^{k_1t_1A} v_{eq} + v_{eq} \equiv 0 , \quad -e^{k_2t_1A} v_{eq} + v_{eq} \equiv 0 .$$

This approximation can be justified from the following point of view. In an actual experiment measurements are only obtained for a finite range of t_1 values. If in this

range relaxation is not significant, then the approximation has some validity. Therefore, with both the pulse approximation and low-relaxation approximation

$$s(t_1, t_2) = ce^{t_2 A}[T_3 e^{k_2 t_1 A} T_2 e^{k_1 t_1 A} T_1(x_0 + v_{eq}) - v_{eq}],$$

$t_1, t_2 \geqslant 0$. In a final simplification step we assume that

$$ce^{tA} v_{eq} = 0, \quad t \geqslant 0.$$

If A_r and R commute this means that

$$0 = ce^{tA} v_{eq} = ce^{tR} e^{tA_v} v_{eq} = ce^{tR} v_{eq}, \quad t \geqslant 0,$$

where we used that $e^{tA_v} v_{eq} = v_{eq}$ for $t \geqslant 0$, as $A_v v_{eq} = 0$. We call this the *uniform relaxation assumption*. This assumption means for example that if the magnetization is coherently aligned with the z-axis, then relaxation to the equilibrium will not introduce any observed magnetization. With this additional assumption we have that

$$s(t_1, t_2) = ce^{t_2 A} T_3 e^{k_2 t_1 A} T_2 e^{k_1 t_1 A} T_1(x_0 + v_{eq}),$$

$t_1, t_2 \geqslant 0$. The two dimensional Fourier transform of s is then given by

$$G(\omega_1, \omega_2) = c(i\omega_2 I - A)^{-1} T_3 P(\omega_1) T_1(x_0 + v_{eq}),$$

$\omega_1, \omega_2 \in \mathfrak{R}$.

5. Example

In this section we consider basic NMR experiments for a weakly coupled spin system consisting of two nuclei of spin $\frac{1}{2}$. The three experiments which we consider were chosen so as to be simple examples of various aspects of the abstract computations which were performed earlier.

5.1. MASTER EQUATION

In this subsection we set up the standard master equation for a weakly coupled two spin system.

Let γ_1, γ_2 be the two gyro-magnetic ratios, s_1, s_2 the shielding constants, B_0 the strength of the strong magnetic field in which the spins are precessing and $\hbar$ Plancks' constant divided by 2π. Let J be the coupling constant and let

$$P_x = \frac{1}{2}\begin{bmatrix} 0 & 1 \\ 1 & 0 \end{bmatrix}, \quad P_y = \frac{1}{2}\begin{bmatrix} 0 & -i \\ i & 0 \end{bmatrix}, \quad P_z = \frac{1}{2}\begin{bmatrix} 1 & 0 \\ 0 & -1 \end{bmatrix}$$

be the Pauli matrices. Set $I_{x1} := P_x \otimes I_2$, $I_{x2} := I_2 \otimes P_x$, $I_{y1} := P_y \otimes I_2$, $I_{y2} := I_2 \otimes P_y$, $I_{z1} := P_z \otimes I_2$, $I_{z2} := I_2 \otimes P_z$. Then the Hamiltonian that stands for the effects of the strong magnetic field is as usual given by

$$H_1 = \gamma_1(1-s_1)\hbar B_0 I_{z1} + \gamma_2(1-s_2)\hbar B_0 I_{z2} + J I_{z1} I_{z2}$$
$$= \frac{1}{2}\begin{pmatrix} \nu_1+\nu_2+\tilde{J} & 0 & 0 & 0 \\ 0 & \nu_1-\nu_2-\tilde{J} & 0 & 0 \\ 0 & 0 & -\nu_1+\nu_2-\tilde{J} & 0 \\ 0 & 0 & 0 & -\nu_1-\nu_2+\tilde{J} \end{pmatrix},$$

where $\nu_i := \gamma_i(1-s_i)\hbar B_0$, $i = 1,2$ and $\tilde{J} = \frac{J}{2}$. Also let $H_{2,1} := \gamma_1\hbar I_{x1} + \gamma_2\hbar I_{x2}$ and $H_{2,2} := \gamma_1\hbar I_{y1} + \gamma_2\hbar I_{y2}$ and assume that the input signals are given by

$$u_1(t) := B_1 \cos(\omega_p(t - t_0 + \Delta t)),$$

$$u_2(t) := B_1 \sin(\omega_p(t - t_0 + \Delta t)),$$

$t \geqslant t_0$, where $\Delta t \geqslant 0$ is a fixed time interval and B_1 is the strength of the radiofrequency field. The measurement operator is given by $M = I_{x1} + I_{x2} + iI_{y1} + iI_{y2}$. The equilibrium density matrix σ^{eq} is given by

$$\sigma^{eq} := \frac{1}{trace(e^{\frac{-1}{kT}H_1})} e^{\frac{-1}{kT}H_1} =: diag(\sigma_1^{eq}, \sigma_2^{eq}, \sigma_3^{eq}, \sigma_4^{eq}),$$

where k is the Boltzmann constant and T the temperature. Moreover let $\hat{R}$ be an unspecified relaxation superoperator. Then the master system can be written as

$$\dot{\sigma}(t) = -i[H_1, \sigma(t)] - i\sum_{j=1}^{2} u_j(t)[H_{2,j}, \sigma(t)] - \hat{R}[\sigma(t) - \sigma_{eq}], \quad \sigma(t_0) = \sigma_0,$$

$$y(t) = trace(M\sigma(t)), \quad t \geqslant t_0.$$

Note that in our setup the condition A2 is satisfied, i.e. $[H_1, \sigma_{eq}] = 0$.

5.2. MASTER SYSTEM IN ERROR VECTOR REPRESENTATION

We now proceed to translate the above master system to the master system in error vector representation. We have that

$$A = -i(I \otimes H_1 - H_1^T \otimes I) - R$$
$$= -idiag(0, -\nu_2 - \tilde{J}, -\nu_1 - \tilde{J}, -\nu_1 - \nu_2, \nu_2 + \tilde{J}, 0, -\nu_1 + \nu_2, -\nu_1 + \tilde{J}, \nu_1 + \tilde{J}, \nu_1 - \nu_2, 0, -\nu_2 + \tilde{J}, \nu_1 + \nu_2, \nu_1 - \tilde{J}, \nu_2 - \tilde{J}, 0) - R,$$

where R is the matrix representation of the relaxation superoperator $\hat{R}$ (we denote by $diag(d_1, \ldots, d_n)$ the diagonal matrix whose diagonal entries are $d_1, \ldots, d_n$). For simplicity of presentation we are going to assume that the matrix representation R of the relaxation superoperator is diagonal, i.e. $R = diag(r_1, r_2, \ldots, r_{16})$. This implies also that the system matrix A is diagonal. Moreover we have that

$$c(vec(M^T))^T = (0\,1\,1\,0\,0\,0\,0\,1\,0\,0\,0\,1\,0\,0\,0\,0)\,.$$

By the representation of the equilibrium density matrix σ^{eq} it follows that

$$v_{eq} := vec(\sigma^{eq}) = (\sigma_1^{eq}, 0, 0, 0, 0, \sigma_2^{eq}, 0, 0, 0, 0, \sigma_3^{eq}, 0, 0, 0, 0, \sigma_4^{eq})^T\,.$$

Therefore $c_0 := cv_{eq} = 0$ and assumption A4 is satisfied. Hence the spin system can be described by the following master system in error vector representation:

$$\dot{e}(t) = Ae(t) + \left(\sum_{j=1}^{2} u_j(t)N_j\right)e(t) + \sum_{j=1}^{2} b_j u_j(t)\,,$$

$$e(t_0) = e_0 := vec(\sigma_0) - v_{eq}\,,$$

$$y(t) = ce(t)\,, \quad t \geqslant t_0\,.$$

5.3. STATE SPACE TRANSFORMATION

Let for $t \geqslant t_0$

$$T(t) := e^{-(t-t_0)i\omega_p P_z} \otimes e^{-(t-t_0)i\omega_p P_z} \otimes e^{(t-t_0)i\omega_p P_z} \otimes e^{(t-t_0)i\omega_p P_z}\,.$$

With the state $r(t) := T(t)e(t), t \geqslant t_0$ the master system in the 'rotating frame' is therefore given by

$$\dot{r}(t) = A_r r(t) + B_1 N_r r(t) + b_r B_1\,, \quad r(t_0) = r_0 := e_0\,,$$

$$y(t) = c_r(t)r(t)\,,$$

where

$$\begin{aligned} A_r := idiag(&0, \nu_2 - \omega_p + \tilde{J}, \nu_1 - \omega_p + \tilde{J}, \nu_1 + \nu_2 - 2\omega_p\,, -\nu_2 \\ &+ \omega_p - \tilde{J}, 0, \nu_1 - \nu_2, \nu_1 - \omega_p - \tilde{J}, -\nu_1 + \omega_p - \tilde{J}, -\nu_1 \\ &+ \nu_2, 0, \nu_2 - \omega_p - \tilde{J}\,, -\nu_1 - \nu_2 + 2\omega_p, -\nu_1 + \omega_p \\ &+ \tilde{J}, -\nu_2 + \omega_p + \tilde{J}, 0) - R\,, \end{aligned}$$

$$\begin{aligned} N_r := \frac{-i\hbar}{2}(&\gamma_2 I_8 \otimes Q(\Delta t) + \gamma_1 I_4 \otimes Q(\Delta t) \otimes I_2 - \gamma_2 I_2 \otimes Q(-\Delta t) \otimes I_4 \\ &- \gamma_1 Q(-\Delta t) \otimes I_8)\,, \end{aligned}$$

$$b_r := N_r v_{eq}\,,$$

$$c_r(t) := e^{(t-t_0)i\omega_p c}\,, \quad t \geqslant t_0\,,$$

with

$$Q(t) = \begin{pmatrix} 0 & e^{-i\omega_p t} \\ e^{i\omega_p t} & 0 \end{pmatrix}, \quad t \geqslant 0 .$$

Note that $B_1 = 0$ describes the situation when no input is applied. In what follows we will consider the following modification of the measured signal

$$y_r(t) := e^{-(t-t_0)i\omega_p} y(t), \quad t \geqslant t_0 .$$

This has the advantage that the frequency range of the signal will be shifted from the MHz range to the Hz and kHz range. The corresponding master system in error vector representation is then given by

$$\dot{r}(t) = A_r r(t) + B_1 N_r r(t) + b_r B_1, \quad r(t_0) := r_0,$$

$$y_r(t) = cr(t), \quad t \geqslant t_0 .$$

5.4. SIMULATIONS

We are going to treat the homonuclear case and therefore assume that $\gamma_1 = \gamma_2 =: \gamma$. We first consider a basic one-dimensional experiment in which a single 90-degree pulse around the y-axis is followed immediately by the detection period. We assume that the spin system is in equilibrium at $t_0 = 0$, i.e. $x_0 = 0$. In Figs. 1(a), 1(b) and 1(c) the results of simulations are shown for a proton spectrum on a 500 MHz instrument. The coupling constant J is $J = 30$ Hz. In Fig. 1(a) a simulation of one-dimensional spectrum is given which is calculated using the pulse approximation. In Fig. 1(b) the same experiment is simulated using the accurate calculations based on Proposition 3 using a strong short pulse. The simulation of the same result is shown in Fig. 1(c) for a soft long pulse. The lack of uniformity of the excitation over the frequency range is clearly seen. The pulse approximation is equivalent to one of the approximations which are assumed in the product operator formulism and in most treatments using density matrix calculations. It is well known that simulations based on such approximations predict uniform excitation over the whole frequency range. It is clearly established in Fig. 1(c) that a simulation based on the analytic solutions presented in Proposition 3 describes the frequency dependence of the excitation and distinguishes between the effects of strong and soft pulses.

In order to demonstrate the use of Lemma 1 we are going to show a simulation of a simple homonuclear J-spectroscopy experiment, where a 90-degree initial pulse around the y-axis is followed by a 180-degree pulse around the y-axis in the middle of the evolution period. In Fig. 2 the spectrum is shown for a weakly coupled spin system with $J = 30$ Hz. The simulation was performed using the accurate formulation for the spectrum.

In the final simulation we consider a basic COSY pulse sequence, i.e. an initial

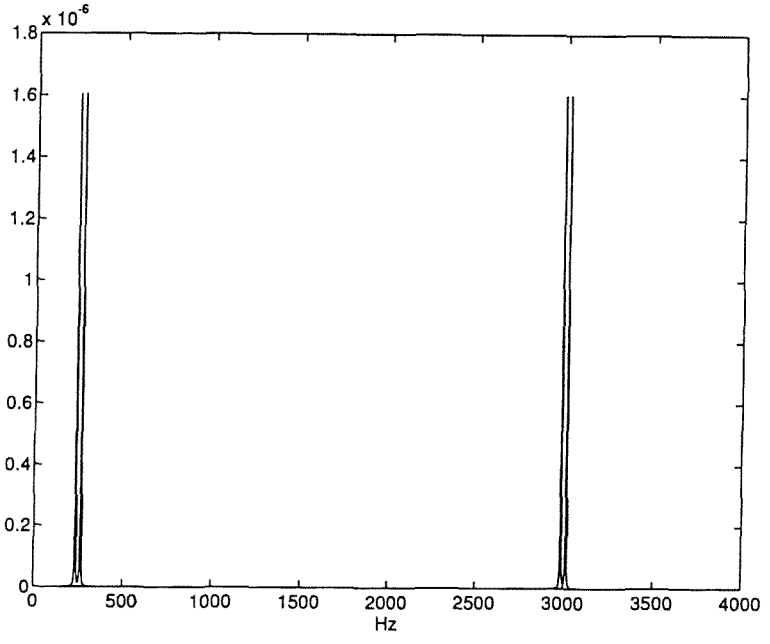

Fig. 1(a). One-dimensional spectrum of a weakly coupled two spin system with coupling constant $J = 30$ Hz, simulated using the pulse approximation.

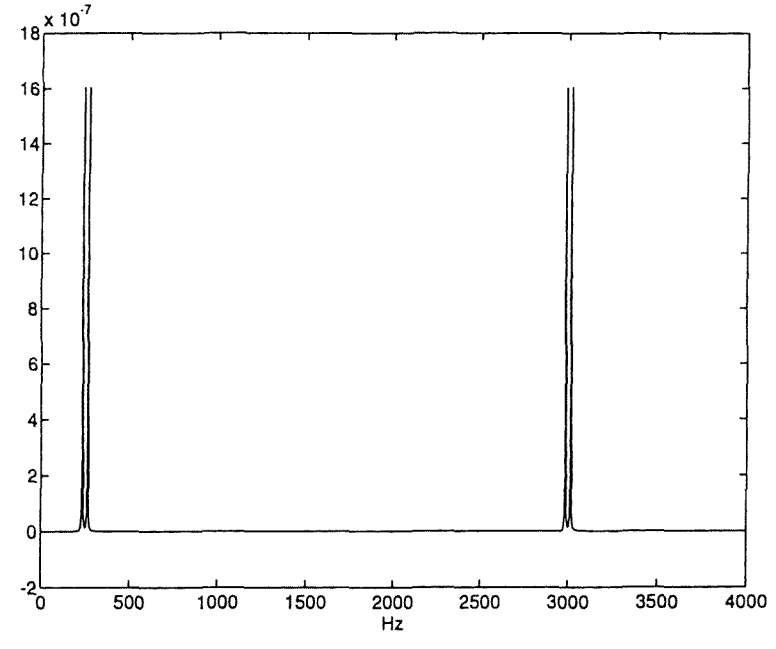

Fig. 1(b). Same spin system as in Fig. 1(a), simulated using accurate calculations, with a short strong pulse.

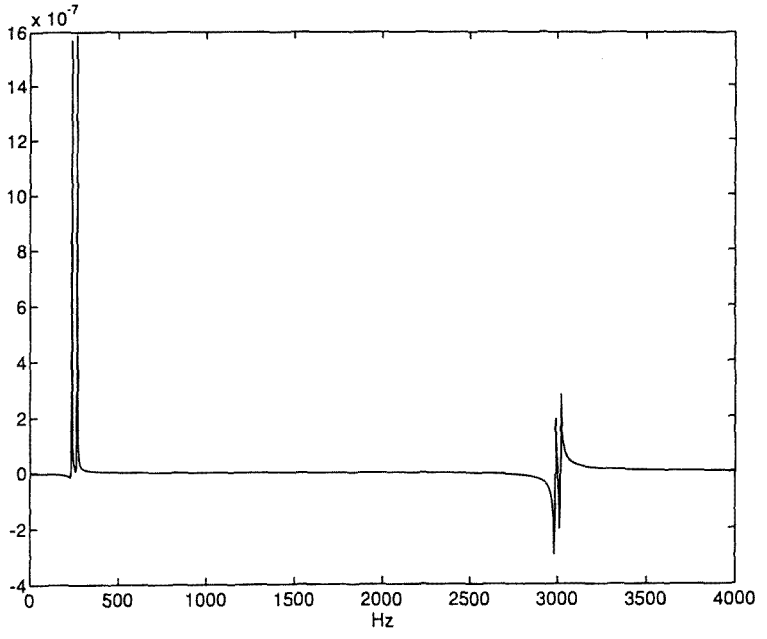

Fig. 1(c). Same spin system as in Fig. 1(b), simulated using accurate calculations, with a long soft pulse.

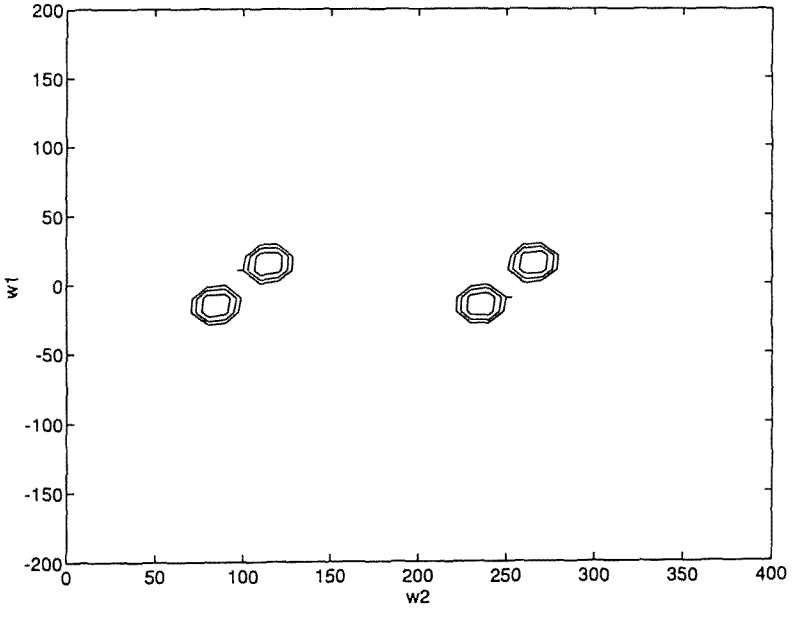

Fig. 2. Two dimensional J-spectroscopy of a weakly coupled two spin system with coupling constant $J = 30$ Hz. The spectrum was simulated based on the accurate calculations.

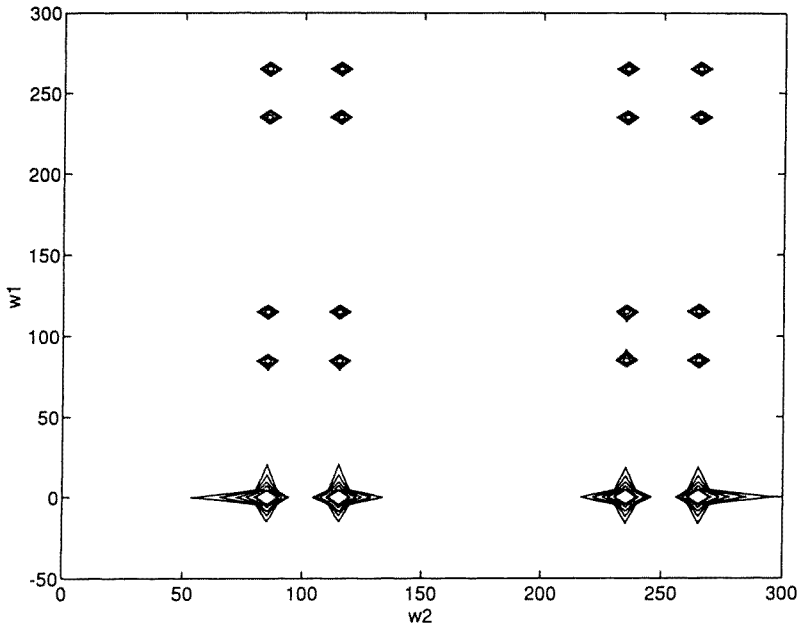

Fig. 3(a). Two dimensional COSY spectrum of the same system as in Fig. 2. The spectrum was simulated based on the accurate calculations.

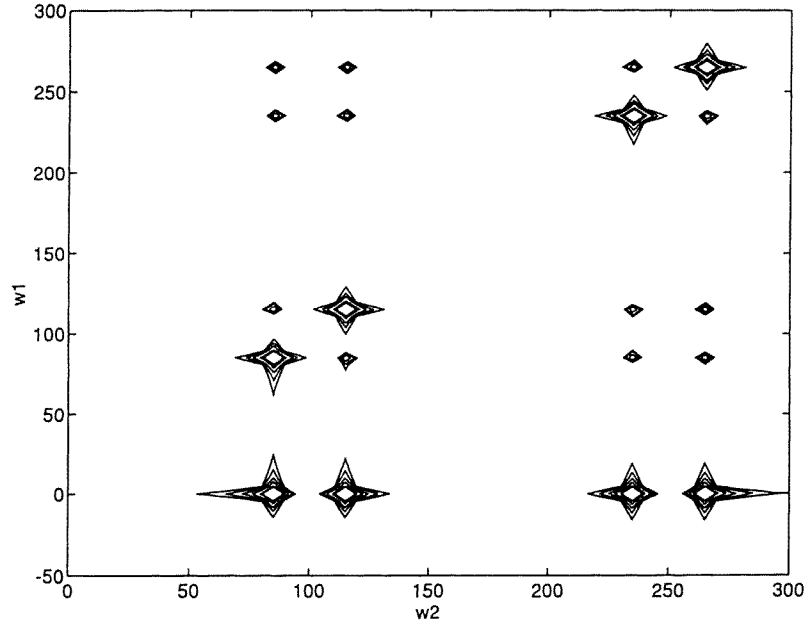

Fig. 3(b). Two dimensional COSY-45 spectrum of the same system as in Fig. 3(a). The spectrum was simulated based on the accurate calculations.

90-degree pulse followed by another 90-degree pulse following the evolution period.

In Fig. 3(a) the COSY spectrum is shown for a weakly coupled spin system with $J = 30$ Hz. It is the same system which was considered in the simulation of the J-spectroscopy experiment. Note the strong axial peaks in the spectrum. The calculation was performed using the accurate description, i.e. without the various approximations. In Fig. 3(b) a COSY-45 experiment is simulated for the same system.

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