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Diffusion coefficient distribution from NMR-DOSY experiments using Hopfield neural network

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Abstract

Diffusion ordered spectroscopy (DOSY) is a powerful two-dimensional NMR method to study molecular translation in various systems. The diffusion coefficients are usually retrieved, at each frequency, from a fit procedure on the experimental data, considering a unique coefficient for each molecule or mixture. However, the fit can be improved if one regards the decaying curve as a multiexponential function and the diffusion coefficient as a distribution. This work presents a computer code based on the Hopfield neural network to invert the data. One small-molecule binary mixture with close diffusion coefficients is treated with this approach, demonstrating the effectiveness of the method.

Keywords: Diffusion coefficient; Inverse problem; Hopfield neural network

1. Introduction

The diffusion coefficient is an important property in studies of mixtures, providing the size and structural information of the particles [1]. In nuclear magnetic resonance, the diffusion ordered spectroscopy, DOSY experiments [2], measure this property of compounds. This technique is based on the application of the gradient field, which encodes and decodes the translational diffusion motion of the components in samples. The signal attenuation is detected and it depends on the gradient strength, the waiting time between the gradients and the diffusion coefficient of the molecules.

In general, the NMR spectrometers work with a fit procedure of the intensity decaying function, providing the diffusion coefficient as a parameter. The distribution function can also be obtained using the inverse Laplace transform. If there is more than one component in the sample with closed diffusion coefficient, the decaying intensity is composed of these contributions and the distribution function concept is more adequate to deal with these problems.

To obtain the diffusion coefficient distribution from these experiments, one has to solve a linear inverse problem [3]. Generally, these inverse problems are classified as an ill-conditioned problem with a decreasing character of the singular values and special methods, e.g., Tikhonov regularization [4,5], truncated singular value decomposition [5,6] and inverse Laplace transform [7], have to be employed.

In this work, an alternative method based on the Hopfield neural network is proposed. Experimental data of an equimolar mixture of Brucine and Isopinocampheol was used to emphasize the applicability of the method. This approach has been also successfully tested to recover the transverse relaxation time distribution from spin-echo experimental data [8], macromolecular properties from light scattering experimental data [9], and the probability density function from experimental positron annihilation lifetime spectra [7].

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2. DOSY—theoretical background

In nuclear magnetic resonance the diffusion motion is studied by the diffusion ordered spectroscopy—DOSY. This technique is based on the application of pulsed field gradient and each infinitesimal volume in the sample is encoded. The angular frequency of nuclear spins depends on its position and the magnetogyric ratio, γ, [10]

$$\omega(r) = -\gamma B(r). \tag{1}$$

The magnetic field gradient is aligned with the principal magnetic field, conventionally in the z direction. The application of the gradient induces a change in the phase angle for each spin as,

$$\phi(z) = \gamma g_z z t, \tag{2}$$

with g_z being the gradient strength and z the coordinate of spin at time t. The total change in the phase angle has another important contribution, related with the principal magnetic field, $\phi(z) = \gamma B_0 t + \gamma g_z z t$.

The pulse sequence in DOSY is similar with the spin-echo experiments. One of the most popular DOSY sequences, the BPPSTE (bipolar pulses with stimulated echo), may be described as follows: two pulsed field gradients with equivalent intensity and opposite signs are applied before and after a hard 180° pulse. This 180° pulse is applied after the first 90° and before the second 90° pulse. This second hard 90° pulse tips the magnetization towards the z-axis, and the molecule then diffuses aligned with main field. After the diffusion delay, a third 90° pulse is issued, followed by the second 180° pulse, flanked by two pulsed field gradients, also with equivalent intensity and opposite signs, aiming at regrouping the magnetization in the transversal plane, resulting in a Hahn-echo [11]. To note a change in the phase angle, the second gradient has to be applied after the spins moved, in a Δ interval. This interval is chosen depending on the diffusion coefficient of the particles.

Within the Δ interval, the change of the phase angle is proportional to the strength of the field gradient. The coherence of the signal is lost and this provides an attenuation of the registered signal. To determine the diffusion coefficient of the particles, a set of experiments has to be realized varying the gradient amplitude. This relation can be expressed by [10,11],

$$I(q) = I_0 \exp(-Dq^2\Delta'), \tag{3}$$

being I the intensity of the signal, D the diffusion coefficient, $\Delta' = \Delta - \delta/3$, with Δ the diffusion time and δ the gradient duration; $q = \gamma g \delta$, with γ being the magnetogyric ratio and g the gradient amplitude.

Generally, the diffusion coefficient is recovered in a specific chemical shift by a fitting procedure of the Eq. (3) and this methodology provides a diffusion coefficient as an appropriate parameter. Nevertheless, if the signal analyzed in the experiment is overlapped, commonly in mixtures, the diffusion coefficients for each component cannot be retrieved.

In a multi-component solution, one has to consider the signals as a sum of several decaying functions [11,12],

$$I(q, v_m) = \sum A_n(v_m) \exp(-Dq^2\Delta'), \tag{4}$$

with $A_n(v_m)$ being the intensity of the signal in NMR experiment at the frequency v_m.

With a continuous distribution of the diffusion coefficients at a particular v frequency, the Eq. (4) can be expressed as,

$$I(s) = \int \exp(-Ds) f(D) \mathrm{d}D, \tag{5}$$

with $s = q^2\Delta'$ and $f(D)$ the distribution function of the diffusion coefficients. The diffusion coefficient distribution has been obtained in NMR spectrometers by the inverse Laplace transform in the CONTIN program [8,10,12]. This code, developed by S.W. Provencher, solves the problem by numerical methods similar to the Tikhonov regularization approach, with the regularization parameter being chosen in a statistic set of data. In this work, the Hopfield neural network was proposed.

3. Inverse problems and Hopfield neural network

In a variety of problems in science, some microscopic properties only can be obtained by the solution of model functions that describes macroscopic experimental data. These model functions, as Eq. (5), are commonly known as Fredholm integral equation. The retrieval of the microscopic property, $f(D)$, from the experimental data, $I(s)$, is an ill-conditioned inverse problem and requires some appropriate techniques to be solved [13].

The standard procedure was adopted to calculate the function **f** in Eq. (5) from data $I(s)$ and $A = \exp(-sD)$. It consist in discretize the variable s in an appropriate interval and convert the integration in a convenient weighted sum to get $\mathbf{Kf} = \mathbf{I}$, being $\mathbf{I} = [I(s_1), I(s_2), \ldots, I(s_m)]^{\mathrm{T}}$, $\mathbf{f} = [f(D_1), f(D_2), \ldots, f(D_n)]^{\mathrm{T}}$ and $\mathbf{K}$ the $(m \times n)$ matrix, defined as

$$\mathbf{K} = \begin{pmatrix} w_1A(D_1, s_1) & w_2A(D_2, s_1) & \ldots & w_nA(D_n, s_1) \\ w_1A(D_1, s_2) & w_2A(D_2, s_2) & \cdots & w_nA(D_n, s_2) \\ \vdots & \vdots & \ddots & \vdots \\ w_1A(D_1, s_m) & w_2A(D_2, s_1) & \ldots & w_nA(D_n, s_m) \end{pmatrix},$$

in which the $w_1, w_2, \ldots, w_n$ are the appropriate coefficients determined by the quadrature to represent the integration equation.

In the Hadamard sense [14], an ill-conditioned inverse problem is established if the solution does not exist, is not unique or continuous in R^n. The decreasing character of the singular values in the $\mathbf{K}$ matrix induces an inverse matrix presenting values bigger than the original one. Therefore, in a problem with $m = n$, if the solution $\mathbf{f} = \mathbf{K}^{-1}\ \mathbf{I}$ is tried, the experimental error in $\mathbf{I}$ matrix is magnified and a wrong answer to the inverse problem is obtained.