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Correlation of transverse relaxation time with structure of biological tissue

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ABSTRACT

Transverse spin-spin relaxation of liquids entrapped in nanocavities with different orientational order is theoretically investigated. Based on the bivariate normal distribution of nanocavities directions, we have calculated the anisotropy of the transverse relaxation time for biological systems, such as collagenous tissues, articular cartilage, and tendon.

In the framework of the considered model, the dipole-dipole interaction is determined by a single coupling constant. The calculation results for the transverse relaxation time explain the angular dependence observed in MRI experiments with biological objects. The good agreement with the experimental data is obtained by adjustment of only one parameter which characterizes the disorder in fiber orientations.

The relaxation time is correlated with the degree of ordering in biological tissues. Thus, microstructure of the tissues can be revealed from the measurement of relaxation time anisotropy. The clinical significance of the correlation, especially in the detection of damage must be evaluated in a large prospective clinical trials.

1. Introduction

Nuclear magnetic resonance imaging (MRI) is a general tool for identifying the structure of both pure compounds and mixtures in liquids [1] or in solids [2]. The properties of spin-spin interactions play an important role in MRI due to the fact that their coupling constant depends on the structural and dynamic parameters of the nuclei and molecules [3,4]. In majority of cases, dipole-dipole interactions (DDI) of nuclear spins are the main interactions which are responsible for spin-spin and spin-lattice relaxation processes. Measurements of the relaxation times allow one to study the dynamic and structural properties of materials and the microstructure and composition of biological tissues [1,5].

The majority of imaging studies of tissue and living organisms is based on the analysis of relaxation times of spins of hydrogen nuclei which are contained mainly in water molecules. While signals from other nuclei may be also used to create images, the high natural abundance and favorable nuclear properties of hydrogen nuclei make them by far the most suitable for producing high-quality images. MRI is a highly flexible technique because the contrast between one tissue and another in an image can be varied simply by the method of detection or the particular pulse sequence used [6,7]. It is possible to produce MR images exhibiting radically different contrasts of patterns by using different approaches such as longitudinal relaxation time weighted (T_1 weighted), density weighted, and transverse relaxation time weighted (T_2 weighted) images [6,7]. The source of the flexibility of MRI lies in the fact that the measured signal depends on properties of the tissue. MRI has been applied in diverse systems such as the study of the human brain [8], microstructure of collagen [9], articular cartilage [10,11], tendon [13–15], kidney, muscle, white matter, and optic nerve [16].

One of the results of these studies was a well-established fact that the transverse relaxation time strongly depends on the orientation of the sample relative to the external magnetic field. This phenomenon is usually attributed to the non-zero averaging of dipolar interactions in water contained between the oriented collagen fibers [10,17]. The collagen fibres form a cavities filled by liquids with characteristic size of few hundred nm [18]. Using the model of a liquid entrapped in nano-size cavities [19–21], it was shown that after averaging over the nanocavity volume, the DDI between any spin pair is determined by a single coupling constant [19–26]. This observation explained why the transverse relaxation time in biological systems depends on a sole angle determined as an angle between the external magnetic field and the direction of the main axis of the cavity [27]. Based on the Gaussian distribution of the directions of collagen fibers represented as a set of

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nanocavities, we have calculated the angular anisotropy of the transverse relaxation time for biological systems: an articular cartilage and a tendon [27]. Good agreement with the experimental data was obtained by adjustment of only one parameter – the standard deviation – which we proposed for characterizing the ordering of collagen fiber orientations [27].

The purpose of the present paper is to establish the correlation between the transverse relaxation time and the standard deviation describing different degrees of ordering the tissue. This paper is organized as follows. In Section 2, for convenience of a reader, we describe the procedure of averaging of DDI between spins inside a nanocavity. Then we consider the transverse relaxation time of dipolar coupling spins. We compare the obtained theoretical results with the experimental data [11] in Section 2. In the last section, we conclude that the relaxation time is strongly correlated with the degree of ordering in biological tissues.

2. Materials and methods

2.1. Averaging of DDI between spins inside nanosize cavities

We consider a system that consists of N nuclear spins, $I = 1/2$, enclosed in an elongated cavity with the principal axes a, b, and $c = b$, and located in an external field $\overrightarrow{H}_0$ directed along the z-axis (Fig. 1). The Hamiltonian which describes the DDI in this system written in units of frequency can be presented as [3]

$$H_{dd} = \gamma_I^2 \hbar \sum_{j>\mu} \frac{1}{r_{j\mu}^3} \left(\overrightarrow{I}_j \overrightarrow{I}_\mu - 3 \frac{(\overrightarrow{I}_j \overrightarrow{r}_{j\mu})(\overrightarrow{I}_\mu \overrightarrow{r}_{j\mu})}{r_{j\mu}^2} \right), \tag{1}$$

where γ_I is the gyromagnetic ratio of nuclei $I, \overrightarrow{I}_j$ is the angular momentum operator of the jth spin, $r_{j\mu} = |\overrightarrow{r}_{j\mu}|, \overrightarrow{r}_{j\mu}$ is the vector connecting the jth and the μth nuclei.

The DDI between spins are weak in comparison with the interaction of a spin with an external magnetic field (the Zeeman interaction). In a high external magnetic field only secular terms of H_{dd} can influence the energy levels to first order, whereas the off-diagonal terms produce a second-order correction. The secular part H_d of the Hamiltonian is given by [3]

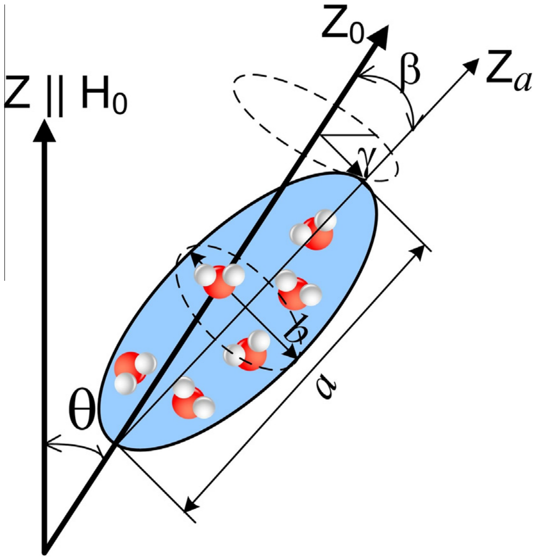

Fig. 1. A nanocavity containing water molecules. θ is the angle between the external magnetic field ($\overrightarrow{H}_0 \| \overrightarrow{z}$) and the Z_0-axis shows an averaged orientation of the nanocavities. β and γ are the polar and azimuthal angles characterizing the deviation of the main axis of a cavity from Z_0.

$$H_d = \gamma_I^2 \hbar \sum_{j>\mu} \frac{1}{r_{j\mu}^3} (1 - 3\cos^2\theta_{j\mu}) \left[I_{zj} I_{z\mu} - \frac{1}{4} (I_{+j} I_{-\mu} + I_{-j} I_{+\mu}) \right], \tag{2}$$

where $r_{j\mu}$, $\theta_{j\mu}, \varphi_{j\mu}$ are the spherical coordinates of the vector $\overrightarrow{r}_{j\mu}, I_{\pm j} = I_{xj} \pm i I_{yj}$. I_{xj}, I_{yj} and I_{zj} are the projections of the spin operator of the jth nuclear spin ($j = 1, 2, \ldots, N, N \geqslant 2$) onto axes x, y and z. In liquids, the molecular motion and rotation are rapid and random, so that we have to average the dipolar Hamiltonian (2) over all the possible directions of the vector $\overrightarrow{r}_{j\mu}$ – the DDI vanishes when we do it. Therefore, in liquids or gases, where molecules are rapidly flipped, the DDI influence is not observed resulting in extreme narrowness of NMR lines [3].

However, the situation for liquids enclosed in nano-size cavities is dramatically different. In a liquid contained in a nano-size volume, due to the restricted molecular motion, the dipolar Hamiltonian (2) may be not averaged to zero, and the spin dynamics is determined by the residual dipolar interaction [19–21].

Estimations show that the dipolar Hamiltonian (2) is not averaged to zero if the typical length of a water-confined cavity is less than $l \simeq 370$ nm [27].

Due to continual tumbling of molecules in liquids, the variables $r_{j\mu}, \theta_{j\mu}, \varphi_{j\mu}$ become time-dependent. To calculate the residual DDI, the exact Hamiltonian (2) has be averaged over time Δt:

$$\overline{H}_d = \frac{1}{\Delta t} \int_0^{\Delta t} H_d(t') dt'. \tag{3}$$

Taking into account the ergodic theorem [12], which states that the time averaging of a random process is the same as the ensemble averaging, we calculate the residual DDI. Replacing the time integration with the integration over spatial coordinates within confined region [21], the spin evolution in a nano-size cavity can be described by the averaged DDI Hamiltonian [20,21]

$$\overline{H}_d = G_d \sum_{j>\mu} (3 I_{zj} I_{z\mu} - \overrightarrow{I}_j \overrightarrow{I}_\mu) \tag{4}$$

with the space-averaged pair coupling G_d for any pair of the jth and μth spins

$$G_d = -\frac{\gamma_I^2 \hbar}{V} P_2(\theta) F(\varepsilon), \tag{5}$$

where $P_2(\theta) = \frac{1}{2}(1 - 3\cos^2\theta)$ is the second-order Legendre polynomial, V is the cavity volume and $F(\varepsilon)$ is the form-factor [21]

$$F(\varepsilon) = \pi \left\{ \begin{array}{ll} \frac{2}{3} + 2\left(\frac{1}{\varepsilon^2} - 1\right)\left(1 - \frac{1}{\varepsilon} \operatorname{arctan} \ \mathrm{h}\varepsilon\right), & a \leqslant b \\ \frac{2}{3} - 2\left(\frac{1}{|\varepsilon|^2} + 1\right)\left(1 - \frac{1}{|\varepsilon|} \operatorname{arctan}|\varepsilon|\right), & a \geqslant b \end{array} \right\} \tag{6}$$

and $\varepsilon^2 = 1 - \frac{a^2}{b^2}, -\frac{4\pi}{3} < F < \frac{2\pi}{3}$. θ denotes the orientation of the cavity with respect to the external magnetic field, $\vec{H}_0$. Estimation shows that the interaction of the spins with the walls of cavity can be neglect for the cavity sizes used in experiments $a = 4.6$ nm and $b = 1.5$ nm [19] because spins near the wall at least 15–20 times smaller than the total number of spins in the cavity.

The averaged DDI Hamiltonian (4) can be rewritten in the following form [21]

$$\overline{H}_d = \frac{G_d}{2} \left(3 I_z^2 - \overrightarrow{I}^2 \right), \tag{7}$$

where $\overrightarrow{I}^2 = I_x^2 + I_y^2 + I_z^2$ is the square of the total nuclear spin operator and $I_z = \sum_{i=1}^N I_{zi}$ is the operator of the projection of the total spin operator onto the z-axis.

Thus, the residual dipolar interaction plays an essential role in the dynamics of a spin system of a liquid in a nanocavity, like the spin dynamics in a solid with an only remarkable difference: