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Spin Relaxation Laws for Quantitative MRI Of Hyperpolarized Spins

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Abstract- **In order to quantify the paramagnetic sources such as oxygen and deoxyhemoglobin in lung and other tissues with MRI of hyperpolarized helium and xenon nuclear spins it is important to understand the relaxation law of these hyperpolarized spins. By means of quantum mechanical calculations we found that the conventional spin relaxation equations are not valid for the hyperpolarized spins. We observed that that the hyper-polarization and spin-coupling result in the multipole spin orders. These multipole spin orders cross-relax each other. New longitudinal relaxation equations for the dipole-dipole coupled hyperpolarized spins at room temperature have been derived. These new equations predict that the longitudinal magnetization relaxation of hyperpolarized spins is, in general, bi-exponential decay instead single exponential decay. The potential applications of the findings in quantitative MRI with hyperpolarized helium and xenon are discussed.**

I. INTRODUCTION

The nuclear spin-polarization is proportional to the magnetic field strength in conventional MRI, so does the signal noise ratio (SNR). The ever-increasing demand on high SNR drives magnetic field strengths of MRI scanners going higher and higher. However, high field strengths make scanners bulky and aggravate the problems such as the magnetic susceptibility artifacts, lengthening of the spin-lattice relaxation time.

Ironically the nuclear spin polarizations at these high magnetic field are really tiny, since the thermal spin polarizations are determined by the Boltzmann factors $\exp(-h\nu/k_B T)$, where T denotes temperature, ν the magnetic transition frequency. Here h is the Planck constant, and k_B is the Boltzmann's constant. The magnetic transition frequencies are radio frequencies (RF) and range from 10^7 Hz to 10^9 Hz in NMR and MRI. The resulted polarizations are about 10^{-6} - 10^{-5} only. On the other hand, the optical photons are much more energetic than the RF-quanta in MRI. The optical transition frequencies are much higher ($\nu \approx 10^{14}$-10^{15} Hz), and the thermal polarizations for optical transitions are of the order of unity. This notion leads to the idea of the optical pumping-assisted MRI [1]. Optical pumping is to use circularly polarized light photons to polarize the atomic electron spins first and then the nuclear spins of noble gases get polarized through the spin exchange between atomic electron spins and nuclear spins. The optical pumping and spin exchange processes result in amazing exchange of nuclear spin polarization due to the angular momentum conservation law. Using optical pumping nuclear spins of noble gases such as ^{3}He and ^{129}Xe can be polarized to 50% or higher at room temperature, hundred thousand times higher than the proton polarization in conventional MRI. MRI of hyperpolarized ^{3}He and ^{129}Xe shows a great potential for clinical applications, especially in the studies of the pathophysiology processes in pulmonary disease and cerebrovascular disease [1-4]. Moreover, the signal noise ratio (SNR) of MRI with hyperpolarized spins is almost independent of magnetic field strength of the scanner. Therefore, relatively inexpensive low field scanners will benefit a lot from the SNR-characteristics of hyperpolarized spins.

As is well known, spin relaxation plays a crucial role in nuclear magnetic resonance (NMR) in general, and the MRI applications especially. Spin relaxation difference between tissue and lesion is the origin of tissue-lesion contrast in MRI images. The relaxation behavior of hyperpolarized spins in living body is very complicated, and is not fully understood yet. There are currently only few published reports on the relaxation of hyperpolarized spins in living bodies [1-4]. It was found that in living body the paramagnetic sources such as oxygen and deoxyhemoglobin play in general a role of relaxation sinks. In addition, the hyperpolarized spins can also cross-relax with other spins (e.g. protons.) The understanding of the exact auto-relaxation behavior of hyperpolarized spins will provide the base-line information for quantifying effects of oxygen and deoxyhemoglobin on relaxation.

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These relaxation laws are critical for implementing functional imaging strategies such as mapping the local oxygen partial pressure in lung or mapping of oxygen concentration in tissue [3, 4]. For example, once the relaxation laws of ^{129}Xe and ^{3}He are known one can conduct a T_1-measurement in ^{129}Xe and ^{3}He MRI to calculate the regional intrapulmonary oxygen partial pressure.

On the other hand, the very nature of the hyper-polarization raises a question if the conventional relaxation laws remain valid, since the conventional relaxation laws are derived from the assumption of weak polarization near the thermal equilibrium. In order to elucidate the relaxation laws, we believe that one should study the auto-relaxation of hyperpolarized spins as the first step. Therefore, in this theoretical work we study the relaxation law of hyperpolarized spins without involvement of the paramagnetic sources, and without the cross relaxation with other spins. In this way, we will be able to show clearly the new features of hyperpolarized spin relaxation.

II. A NEW LOOK AT RELAXATION LAWS

At first glance one would not expect a different relaxation law for hyperpolarized spins if no paramagnetic source were involved. In fact, in current literature [1-4] it is implied that spins would obey the same relaxation equations regardless if the spins were thermally polarized or hyperpolarized. As is well known, for the thermally polarized spins without cross-relaxation with other spins, the longitudinal magnetization always relaxes exponentially toward the thermal equilibrium magnetization. However, we do not expect that this relaxation law holds true for hyperpolarized spins, based on the following two observations. First, the conventional spin relaxation laws are derived with the assumption of spins states being near thermodynamical equilibrium. This assumption is not true any more for the hyperpolarized spins. In fact, the conventional spin relaxation laws are derived under three important assumptions [5, 6]. The first assumption is the high temperature approximation, which assumes that $\beta\omega \ll 1$, where $\beta = h/(2\pi k_B T)$, here T is the lattice temperature in K, and $\omega/2\pi$ is the Larmor frequency of the spins in a magnetic field B_0. In the conventional MRI $\beta\omega$ is in the order of 10^{-5}. The second assumption is that the spins are near thermodynamical equilibrium, or more accurately, it is assumed that $\left|Tr\left[\left(\sigma - \sigma_{eq}\right)\cdot I_z\right]\right|$ is always less than or comparable to $\left|Tr\left(\sigma_{eq}\cdot I_z\right)\right|$, where σ is the density operator of the spins, σ_{eq} the density operator at the thermodynamical equilibrium, I_z the z-component spin operator and the operator T_r stands for the trace operation. The third assumption is that the magnetic field B_0 is much larger than the random magnetic field generated by the spin-spin interactions. In the conventional MRI, these three assumptions are met, but for the MRI with hyperpolarized spins the second assumption will not hold true any more, because the hyper-polarization state is far away from the thermodynamical equilibrium at the room temperature, and $\left|Tr\left[\left(\sigma - \sigma_{eq}\right)\cdot I_z\right]\right|$ can be much larger than $\left|Tr\left(\sigma_{eq}\cdot I_z\right)\right|$. Therefore, the conventional spin relaxation equations may not be valid for the hyperpolarized spins.

Second, as is shown below, there exist the multipole spin orders with hyperpolarized spins. For thermally polarized spins, the magnetic order is the dipolar order representing by conventional magnetization vector.

III. HYPER-POLARIZATION AND MULTIPOLE SPIN ORDER

We observed another important difference between the hyperpolarized state and the thermal equilibrium state: difference in the spin orders. It is well known, spins of I =1/2 at the thermal equilibrium in a magnetic field B_o along the z-axis are dipole-polarized, and the density operator σ_{eq} of two coupled spins is

$$\sigma_{eq} = \frac{1}{4}1_O + \frac{1}{4}\beta\omega I_z \qquad (1)$$

where 1_O is the unity operator. However, hyperpolarized spins have not only large dipolar spin order, but also multipole spin orders. A density matrix operator of two coupled spins hyperpolarized along the z-axis can be expanded as

$$\sigma = \frac{1}{4}1_O + B_1 I_1^z + B_2 I_2^z + B_3 I_1^z I_2^z \qquad (2)$$

Equivalently for the coupled spin system we can rewrite Eq. (2) as:

$$\sigma = \frac{1}{4}1_O + C_1 I_z + C_2 Q_0 + C_3 (I^2 - I_1^2 - I_2^2) \tag{3}$$

where the coupled spin vector $\vec{I} = \vec{I}_1 + \vec{I}_2$ and Q_0 is the quadrupole moment of the coupled spins

$$Q_0 = 3I_z^2 - I^2 \tag{4}$$

In Eq. (3) $(I^2 = I_1^2 = I_2^2)$ is the invariant spin-order. The B_i and C_i are constant expansion coefficients. In fact, for the completely polarized state with a 100% polarization, we find out

$$\sigma_{100\%} = \frac{1}{4}1_O + \frac{1}{2}I_z + \frac{1}{6}Q_0 + \frac{1}{6}(I^2 - I_1^2 - I_2^2) \tag{5}$$

Therefore, the multipole spin-order expansion coefficients for a state hyperpolarized along the z-axis are C_1 = 1/2, C_2 = 1/6, C_3 = 1/6. Obviously, for a strongly hyperpolarized state $C_i >> \beta\omega \approx 10^{-5}$. It should be noted that while the dipolar spin order I_z can be visualized as a vector, the multipole spin orders can only be visualized in multidimensional quantum state space. More specifically, in a spin state subspace spanned by the three spin orders: dipole order I_z, quadrupole Q_0 and invariant order $(I^2 = I_1^2 = I_2^2)$, the states of thermally polarized spins are all limited to a tiny one-dimensional linear section (along I_z) around to the origin. In contrast the states of hyperpolarized spins occupy a much larger three-dimensional volume defined by Eq. (3) (Figure). This much larger three-dimensional state space contributes to new relaxation mechanism as we show as follows.

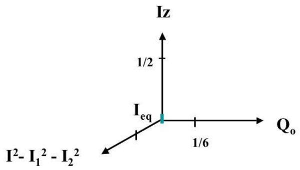

Figure. The quantum state space for hyperpolarized spins.

IV. THE NEW RELAXATION LAWS FOR HYPERPOLARIZED SPINS

In this work we assume that the spin-spin interaction between hyperpolarized spins is the dipole-dipole coupling with no correlation between different spin pairs. The derivations that follow can be extended to cases with other relaxation mechanisms.

As is well known that in quantum statistical mechanics a state of spin system can be described by a density operator [5-6]. The dynamics of the spin system is determined by the equation of motion of the density matrix operator for the spin system

$$\hbar \frac{d\sigma}{dt} = -\mathrm{i}[\mathrm{H}_0 + \mathrm{H}_1, \sigma] \tag{6}$$

where H_0 is the Zeeman-Hamiltonian for spins representing the well-known Zeeman coupling between spins and magnetic field of the MRI scanner and H_1 is the perturbing Hamiltonian representing the random spin-spin interaction. As is explained before, in this work H_1 will be the dipole-dipole coupling Hamiltonian, which can be written using products of the irreducible tensor operators of the spin and lattice [ref]. For H_0, note that ^{3}He's gyromagnetic ratio is 76% of proton's and that of ^{129}Xe is 28% of proton's only. *r* the length of vector **r** connecting the two spins.

Integrating Eq.(1) by successively approximations up to the second order in H_1 following Hubbard 's approach [5, 6], and after tedious calculations we find the new relaxation law :

$$\begin{aligned} &< I_z(t) >= \exp(=t/T_1) < I_z(0) > \\ &+ [1 = \exp(=t/T_1)] I_{eq} (1 + \frac{2}{3} < I^2 = I_1^2 = I_2^2 >) \\ &+ \frac{T_1 T_Q}{T_{IQ}(T_Q = T_1)} [\exp(=t/T_1) = \exp(=t/T_Q)] < Q_0(0) > \end{aligned} \tag{6}$$

where the assembly average of a multipole order $< O >= Tr[\sigma(t) \cdot O]$, such as $< I_z(t) >$ and $< I_z(0) >$ are the values of the longitudinal magnetization at times t and t=0, respectively, and $< Q_0(0) >$ is the quadrupole-order value at t=0. Instead of a single relaxation time for the longitudinal magnetization $< I_z(t) >$ the relevant relaxation times in conventional MRI with protons here are there relation times. In addition to the conventional longitudinal relaxation time

$$\frac{1}{T_1} = \frac{1}{4}[J_1(\omega) + 4J_2(\omega)] \qquad (7)$$

$< I_z(t) >$ is affected by the relaxation times T_Q for the quadrupole order and the dipole-quadrupole cross–relaxation time T_{QI} as well, and they are given by:

$$\frac{1}{T_{QI}} = -\frac{3}{8}\beta\omega J_1(\omega) \qquad (8)$$

$$\frac{1}{T_Q} = \frac{3}{4}J_1(\omega) \qquad (9)$$

In Eqs. (7-9) the conventional spectral functions $J_m(\omega)$ represent the power-spectra of the random movement of the lattice [5]. The specific functional forms of $J_m(\omega)$ are determined by the details of the relaxation mechanism such as random spin translations and/or rotations [5].

Note that for the conventional thermally polarized spins, such as proton-MRI

$$< Q_0 >=< I^2 = I_1^2 = I_2^2 >= 0 \qquad (10)$$

In this case Eq. (6) becomes the familiar, conventional longitudinal magnetization relaxation equation, Thus, Eq.(6) is indeed the generalization of the single exponential decay law to the spins with arbitrary initial polarization at high temperatures. According to Eq.(6) $< I_z(t) >$ will relax in a bi-exponential decay.

The two-component decay will manifest themselves explicitly for some common pulse sequences encountered in MRI. For example, if at t=0 a short 90° RF-pulse along the x-axis is applied to hyperpolarized xenon or helium spins, then $< I_z(0+) >= 0$, but due to the hyper-polarization one still has large quadrupole-order $|< Q_o(0+) >| >> \beta\omega$ for hyperpolarized spins because of Eq. (4). It is then clear from Eq. (6) that the longitudinal magnetization $< I_z(0+) >$ will evolve according to

$$< I_z(t) >= [1 = \exp(=t / T_1)]I_{eq}(1 + \frac{2}{3} < I^2 = I_1^2 = I_2^2 >)$$

$$+ \frac{T_1 T_Q}{T_{IQ}(T_Q = T_1)}[\exp(=t / T_1) = \exp(=t / T_Q)] < Q_0(0) >$$

$$(11)$$

Note that in Eq. (11) the equilibrium magnetization $I_{eq} \propto \beta\omega$ and the quadrupole-dipole cross-relaxation rate $1/T_{QI} \propto \beta\omega$ as well. Since $|< Q_o(0+) >| >> \beta\omega$, hence Eq. (11) dictates a bi-exponential decay for the longitudinal magnetization $< I_z(0+) >$, as the two decay components have comparable amplitudes and different decay rates. In addition, Eq. (11) also predicts that after relaxing for a long time $< I_z >$ will reach the steady state value I_{Zss}:

$$I_{Zss} = I_{eq}(1 + \frac{2}{3} < I^2 = I_1^2 = I_2^2 >) \qquad (12)$$

For the thermally polarized spins, $\left\langle I^2 = I_1^2 = I_2^2 \right\rangle$ is equal to 0, thus $I_{Zss} = I_{eq}$, as is expected. However, for hyperpolarized spins, $\left\langle I^2 = I_1^2 = I_2^2 \right\rangle$ is larger than 0, thus Eq. (12) predicts surprisingly that $I_{Zss} > I_{eq}$. Note that Eq.[26] holds as long as $\left\langle I^2 = I_1^2 = I_2^2 \right\rangle$ is a constant in time. If there is a cross-relaxation of the hyperpolarized spins with other species of spins[8], then $<I^2 - I_1^2 - I_2^2>$ may not be a time-constant

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V. DISCUSSIONS AND CONCLUSIONS

The spin states (spin orders) and spin relaxation are among the most important aspects of a spin system that can be utilized in MRI. Although the spin states and relaxation laws of conventional thermally polarized spins are well known, one cannot assume that the same laws dictate behavior of hyperpolarized spins. In this work we find out new spin states (multipole spin orders) and new relaxation laws. New longitudinal relaxation equations for the dipole-dipole coupled hyperpolarized spins have been derived. These new relaxation equations predict that the longitudinal magnetization relaxation for hyperpolarized spins is, in general, bi-exponential decay instead single exponential decay. Though with this limited scope of the autorelaxation of hyperpolarized spins, our findings are still of significance to clinical applications of hyperpolarized spins. First of all, understanding of the exact auto-relaxation behavior of hyperpolarized spins will provide the base-line information for quantifying effects of oxygen and hemoglobin on relaxation. For example, once the auto-relaxation laws of ^{129}Xe and ^{3}He are known one can conduct a T_1-measurement in ^{129}Xe and ^{3}He MRI to calculate the regional intrapulmonary oxygen partial pressure. In other words, our theoretical study has potential application in implementing functional imaging strategies such as mapping the local oxygen partial pressure in lung or mapping of oxygen concentration in tissue.. Second, our theoretical study will provide understanding of hyperpolarized spin relaxation in bio-compatible media. Currently most of MRI applications with hyperpolarized spins in living body are based on the inhalation approaches [1-4]. Inhaled hyperpolarized spins are taken up by the pulmonary blood and distributed throughout the body. The signals of hyperpolarized spins in distal organs are thus limited by the dilution and decay during the transport. In order to increase the effectiveness of hyperpolarized spins as MRI probes, one may try to directly inject hyperpolarized spin-saturated bio-compatible medium (e.g. Perfluorocarbon emulsions) into the body instead of using the inhalation approach [3]. Obviously correct modeling of ^{129}Xe and ^{3}He transport from delivery to final distribution of polarization in the target tissue calls for more accurate understanding of the auto-relaxation behavior of hyperpolarized spins in bio-compatible media and tissue. Finally, the recently discovered SPINOE (spin polarization induced nuclear Ovehauser effect [8]) find many applications in medical imaging and material science [8]. Our study lays down a frame work for accurate modeling SPINOE, namely the cross relaxation between hyperpolarized spins and other spins such as protons and carbons.

In examining the auto-relaxation laws of hyperpolarized spins, we find new spin states (multipole spin orders) and new relaxation law. The role of the transverse multipole spin orders should also be explored in our future works. Our work shows that hyperpolarization provides us much more that just hyper-magnetization. There exist new dimensions in hyperpolarized spin physics as shown in this work. These new dimensions have great potential to bring more new MRI techniques for clinical applications.

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