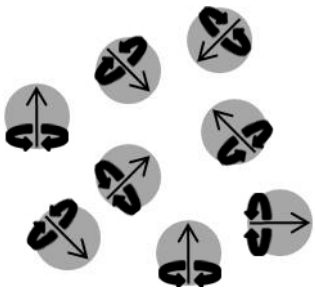
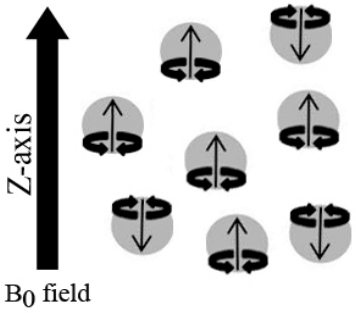
Introduction

MRI is a powerful noninvasive diagnostic technique, which is used to generate magnetic field (B_0) and interacts with spin angular momentum of the nucleus in the tissue. Spin angular momentum depends on number of protons and neutrons of nucleus. Nuclei with even number of protons plus neutrons are insensitive to magnetic field. So cannot be viewed by MRI. We can think of each nucleus as an arrow with arbitrary direction in absence of external magnetic field FIGURE. And we consider them to get oriented in same direction once magnetic field applied FIGURE. In order to get nuclei orient in specific direction, energy is supplied, and to bring it to original position energy is emitted. All this transitions eventually lead to changes in angular velocity, which is defined as Larmor frequency and expression for which is $\omega = \gamma B_0$ (γ is the gyromagnetic ratio). It is not easy technique to detect energy, which involved in such a transition, that's why use of high resolution spectrometers required, those which are developed by nowadays as a most powerful MRI are close to 9 Tesla with mass approaching forty five tons. Unfortunately it is expensive tool to purchase and to operate. That's why new techniques should be developed, so most of the MRI spectrometers can be involved in imaging. Fortunately presence of huge amount of nuclei in analyzed sample or body can provide with some information.



Nucleus in absence of magnetic field

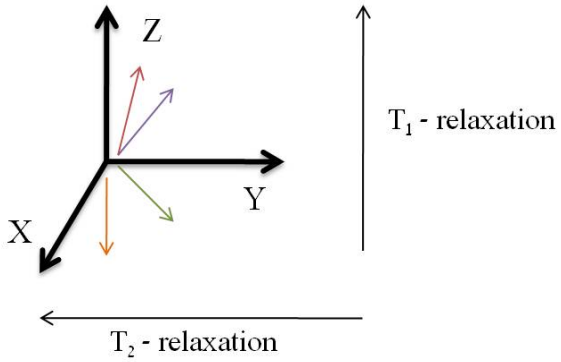


Nucleus in presence of magnetic field

Nuclear magnetic resonance relaxometer

Each nucleus possesses microscopic magnetic spins of *x*, *y* and *z*. Presence of randomly distributed atoms with varying *x* and *y* spins will lead to zero upon summation of *x* and *y* planes. But in case of *z*, summation of magnetic spins will not lead to cancellation. According to Currie's law, which is $M_z = CB_0/T$ (M_z is the resulting magnetization of *z* axis, C is a material specific Curie constant,

B_0 is the magnetic field, T is absolute temperature), magnetization of *z* axis proportional to magnetic field applied from outside. Basically, excitation happens by passing current through coil which leads to magnetization of *x*, *y* and *z* axis. It is the way of changing magnetism from *z* axis to *x* and *y* axis. Once external current supply is turned off, magnetization will eventually quench. Which means change of magnetization from x and y axis to *z* axis, were it eventually become equilibrated and device no more can detect the signals. Energy which is emitted from excited spin leads to development of new current inside of the same coil recorded by detector; hence same coil can be used as detector and source of magnetic field. This process called as a relaxation and that's why, return of magnetization to *z* axis called as spin-lattice relaxation or T_1 relaxation (time required for magnetization to align on *z* axis). Eventual result of zero magnetization on *x* and *y* axis called as spin-spin relaxation or T_2 relaxation FIGURE.



Magnetic spins relaxation mechanism

Contrast agents for MRI

In MRI image contrast determined according to T_1, T_2 or the proton density parameters. There for we can obtain three different images. By changing intervals between radio frequency (RF) 90° pulses and RF 180° pulses, desired type of image can be obtained. There are few computational techniques available to improve contrast of image; those are repetitive scans and different mathematical computations. Repetitive scans take long time, therefore cannot be applied in MRI. Mathematical computation on their own, do not provide with desired results. For that reason, in order to obtain high resolution images, contrast agents (CA) are important part of medical imaging.

Types of contrast agents

There are different types of contrast agents available in markets which are basically, reduce supremacy of T_1 or T_2 and differentiate according to relaxivity$_1$ (r_1) and relaxivity$_2$ (r_2) values. The relaxivity (r_i) can be described as $1/T_i$ (s^{-1}) of water molecules per mM concentration of CA. Contrast

agents are paramagnetic and can interact with dipole moments of water molecules, causing fluctuations in molecules. This theory is known as Solomon-Bloembergen-Morgan (SBM) theory. Those which are efficient were Gadolinium, Iron and Manganese cations. Fundamentally the role of contrast agents can be played by any paramagnetic species.

Principal of interactions of CA with surrounding media

There are two main principles of interactions of contrast agents with water molecules. One is direct interaction, which is called inner sphere relaxation, and another mechanism happens in absence of direct interaction with water molecule which is outer sphere relaxation. If we have water molecules in the first coordination sphere of metal ion, we can consider them as the inner sphere, and if diffusion of protons from outside happens randomly we define them as outer sphere relaxation. Another type of relaxivity comes from already affected water molecules, which transfers their relaxivity to protons of close proximity, this type of relaxivity called second sphere and is usually neglected or contributed as outer sphere. In inner sphere proton relaxivity there are two main mechanisms involved in relaxation. One is dipole-dipole interactions between metal and proton and another is scalar mechanism. Dipole-dipole interaction affects electron spin vectors and scalar mechanism usually controls water exchange. Effect of contrast agents on T_1 relaxation is much larger than on T_2, since T_1 is much larger for tissues than T_2.

Determination of relaxivity

Determination of relaxivity became very easy with the advancements of NMR and computer technology, where you need just to load your sample and read values from the screen. But let's consider in more detail what are the precautions should be taken during sample preparation and data acquisition.

Sample preparation

Sample to be analyzed is dissolved in water or any other solvent. We use water since contrast agents for MRI are used in aqueous media. Amount of solution you use determined according to the internal standard volume, which is used for calibration purposes of device and is usually provided by company producing device. A suitable sample holder is a NMR tube, they are also determined according to the devise you are using, since each device may have different diameter of tube holder compartment and the material they are made up of is glass. It is important to degas solvent prior measurements by bubbling gas through it (nitrogen or argon works well), so no any traces of oxygen remains in solution, since oxygen is paramagnetic.

Data acquisition

Before collecting data it is better to keep sample in device compartment for few minutes, so temperature of magnet and your solution equilibrates. Data you will have after measurements on your sample is the T_1 or T_2 value, which will depend on what you did request from device to measure. The relaxivity (r_i) calculated according to EQUATION, where T_i is the relaxation time in the presence of CAs, T_{id} is the relaxation time in the absence of CAs, and [CA] is the concentration of paramagnetic CAs (mM). So having the relaxivity values you can compare your compound to other contrast agents.

$$r_i = (1/T_i - 1/T_{id})/[CA]$$

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