MEASUREMENT OF DIFFUSION COEFFICIENTS BY NUCLEAR MAGNETIC RESONANCE

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ABSTRACT

This paper deals with the assesment of molecular diffusion coefficients by nuclear magnetic resonance. The pulse sequence of spin echo with two symmetrical "diffusion" gradients is explained here and also the influence of its parameters on measuring accuracy is mentioned.

1 INTRODUCTION

Nuclear magnetic resonance in material spectroscopy and medicine tomography is a method that has been known for a long time. Nowadays new methods are being developed, which extend the original facilities of NMR. One of these methods is also the assessment of diffusion coefficients. This method can be used for medicine diagnostics and for indirect measurement of material diffusion. The diffusion in some chemicals and in most biological structures is strongly dependent on direction, so it is a tensor. When the tensor quantity is measured, it is necessary to find 6 independent components.

2 NMR SIGNAL

Let us consider the basic NMR experiment, when nuclei of a substance are irradiated by a 90 ° radiofrequency pulse ($\pi/2$ pulse). The sample is characterized by its gyromagnetic ratio γ and it is placed into a homogenous magnetic field $\boldsymbol{B_0}$, which has the z-axis direction. If there is no other signal affecting the sample, macroscopic longitudinal magnetization $\boldsymbol{M_0}$ will be set up in the sample (absolute temperature must be greater than zero). The build-up of longitudinal magnetization takes a certain time called spin-lattice relaxation time, denoted T_1. The microscopic approach shows that NMR active nuclei (nuclei with $\pm 1/2$ spin) placed into homogenous mag. field $\boldsymbol{B_0}$, start to rotate and do a precession motion about the z-axis with angular frequency ω_0.

This frequency is called the *Larmor frequency* [1] and it is given by this linear formula:

$$\omega_0 = -\gamma \cdot B_0 . \qquad (1)$$

Because the nuclei rotate about the *z*-axis, the net magnetization $\boldsymbol{M_0}$ is parallel to this axis and the components of *xy*-plane are zero.

If we irradiate the sample, by a 90 ° rf pulse $\boldsymbol{B_1}$, in *xy*-plane, the vector $\boldsymbol{M_0}$ starts to fall in a spiral into *xy*-plane (Fig. 1.a). It is convenient to use the rotating coordinate system which rotates about the *z*-axis at the Larmor frequency ω_0, where a rotating vector at ω_0 appears stationary. The magnetization vector $\boldsymbol{M_0}$ in the rotating frame falls after the circular path direct to the *xy*-plane (Fig. 1b).

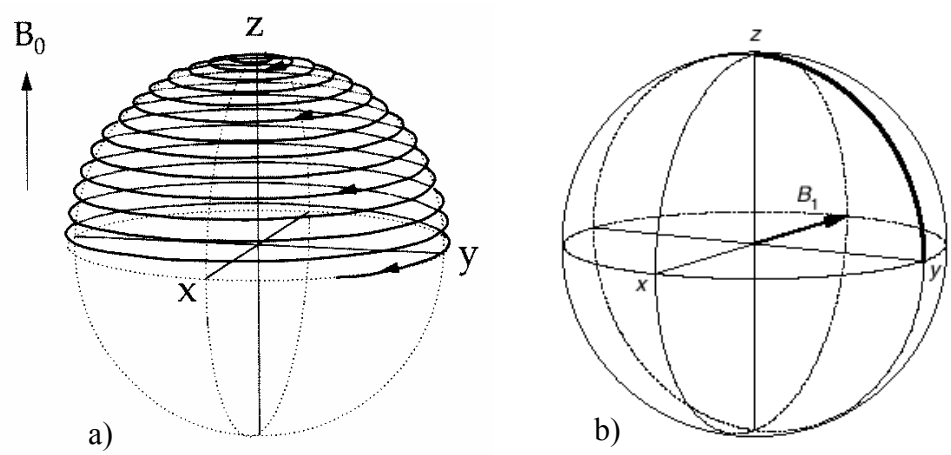

Fig. 1: *Path of magnetization vector M_0 : a) laboratory coordinate system, b) rotating coordinate system*

After the end of 90 ° pulse, the net magnetization vector $\boldsymbol{M_0}$ starts to return back to initial state, at a rate given by the spin-lattice relaxation constant T_1. Additionally, due to the influence of atoms and their neighbourhood (electron motion, diffusion, coupling, etc) inhomogeneities arise in basic field $\boldsymbol{B_0}$. This causes the detected signal consists of waves with different frequencies [1]. So some nuclei have frequencies little bit higher and some little bit lower than ω_0. Therefore the receiving coil receives the sum of all waves and the resulting signal decays in time, because the waves are not coherent (see Fig. 2).

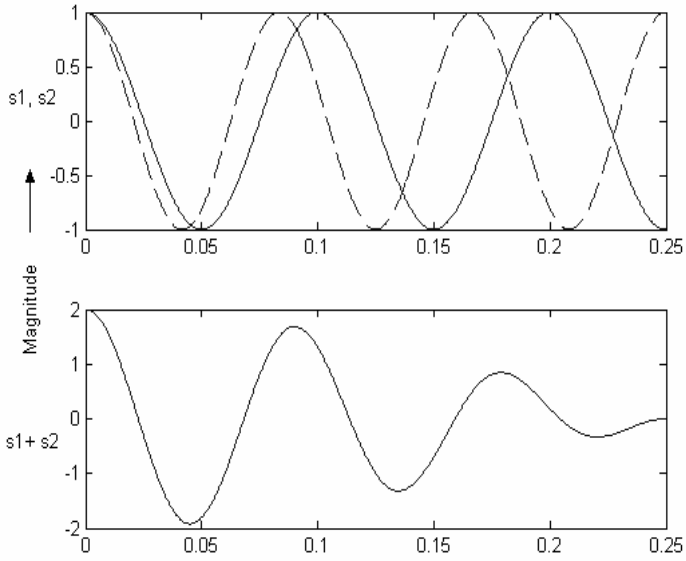

Fig. 2: *FID - impact of incoherence spins.*

The bulk of this decay characterises the spin-spin relaxation time T_2 (T_2 is always less than T_1). The resulting signal is called the *free induction decay* (FID) and it has the shape of an exponentially decaying cosine function [1], mathematically described by

$$y(t) = M_0 \cdot \cos(\omega_0 t) \cdot e^{\frac{-t}{T_2}}. \qquad (2)$$

The nuclei rotating about the *z*-axis at the same velocity as the rotating frame will appear stationary there (Fig. 3.B). The nuclei that rotate faster or slower will turn round there (see in Fig. 3.C) and then the signal decays - according to equation (2).

The basic experiment could be simply extended by another radiofrequency pulse. It is called 180 ° pulse, because it rotates the nuclei 180 ° about the *y*-axis (Fig. 3.A). This causes that faster nuclei are decelerated (or slower nuclei are accelerated) and they will be in phase (see Fig 3.D). The spins are completely re-phased (will be in phase) after the time of TE/2 (TE Time of Echo) and further in time they are de-phasing again as ordinary FID does. This *echo*, as this specific signal is called, actually consists of two FIDs and is located far from the 180 ° pulse, which is a great advantage of this sequence from the viewpoint of distortion [2].

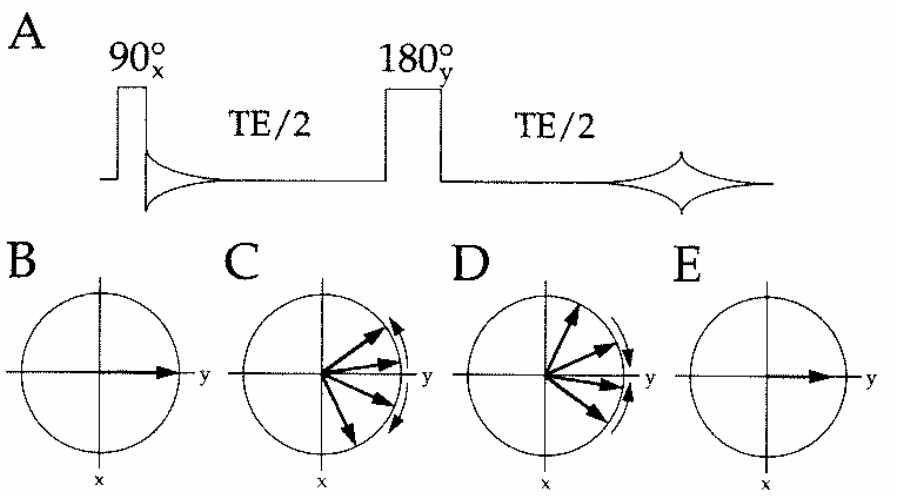

Fig. 3: *Spin echo: a) pulse sequence, b-e) time-vector diagram (rotating frame – xy plane)*

3 DIFFUSION

Diffusion is a random translational motion of molecules caused by thermal energy. It is expressed by the diffusion coefficient *D*, which determines the mean distance *y*, passed by molecules at time t_d

$$\left(y^2\right) = 6 \cdot D \cdot t_d. \qquad (3)$$

Coefficient *D* (usually given in mm^2/s) expresses the rate of molecular mobility of a certain substance. During the observation time t_d molecules can migrate between areas with different diffusion coefficients, which cause dependence on time t_d. The Apparent Diffusion Coefficient ADC was established in practice for these cases. It is the effective value of diffusion and it is time-independent. ADC is often anisotropic (different in direction) and therefore it is a tensor composed of 6 independent components.

3.1 ASSESMENT OF DIFFUSION BY NMR

The magnitude of MR signals in a gradient magnetic field depends (among others) on molecular motion in an observed sample [1]. If two additional gradients are added to the pulse sequence in Fig. 3, symmetrically around the 180 ° pulse, the speed of precession is spatially dependent [2]. When the nucleus changes its position (facing the gradient), while the signal is measured, the magnitude of local magnetic field is different and the nucleus cannot be re-phased exactly. Therefore the spin echo signal does not reach the same value as in the case of fixed nuclei. The diffusion coefficient D can be obtained from that difference. The signal magnitude is exponentially dependent on the diffusion coefficient according to the following equation defined for the pulse sequence in Fig. 4 [3]

$$S \approx S_0 \cdot e^{-bD} \approx S_0 \cdot e^{-\gamma^2\delta^2G^2\left(\Delta-\frac{\delta}{3}\right)D}, \qquad (4)$$

where G is the amplitude of gradient pulses and δ their length, Δ is the time distance between grad. pulses (Δ – δ/3 is diffusion time t_d), S_0 is the signal measured without gradients. Parameter b in the exponent of equation (4) is called the *multiplication factor b* and expresses sequence sensitivity to diffusion measurement. For sufficient sensitivity it is necessary for the b-factor to be at least hundreds s/mm^2 [3]

$$b = \gamma^2 \cdot \delta^2 \cdot G^2 \cdot \left(\Delta - \frac{\delta}{3}\right). \qquad (5)$$

The experiment in Fig. 4 is actually a spin-echo sequence extended by two gradient pulses placed symmetrically around the 180 ° pulse. When the influence of relaxation time T_1 is neglected (single measurement or repetitive measurement with sufficient breaks to relaxation) equation (4) could be written in the form:

$$S = S_0 \cdot e^{-b\cdot D} \cdot e^{-TE/T_2}. \qquad (6)$$

According to equation (6), is the magnitude of gradient G essential to reach sufficient value of b-factor. However, the value of gradient is technically limited and further increasing of the b-factor is possible only by extending the gradient duration or the distance between them. Both these possibilities lead to increasing time TE and accordingly decreasing the signal due to relaxation time T_2 (as follows from (6)). For this reason, this sequence is not appropriate for experiments with short relaxation time T_2.

3.2 EXPERIMENT

The measurement was performed on a 4.7 T spectrotomograph at the Institute of Scientific Instruments AS CR in Brno, with a sample of distilled water. The pulse sequence of spin echo with two symmetrical gradients was used. In the first the amplitude of spin echo without optimal parameters (δ,Δ,G) was measured. This measurement was affected by considerable error, the computed value of diffusion coefficient D was completely incorrect (10^3 times greater than real value). Optimal setting of parameters (see below) was found experimentally, with the error not exceeding 10 %.

Optimal parameters:

- amplitude of diffusion gradient G = 12.6 mT/m
- distance between leading edges Δ = 6 ms
- duration of diffusion gradient δ = 20 ms

The ramp time of gradient pulses should be as short as possible. The first two parameters (G,Δ) have a strong effect on measurement accuracy. However the sequence with these parameters is not universal for other relaxation times T_1 and T_2.

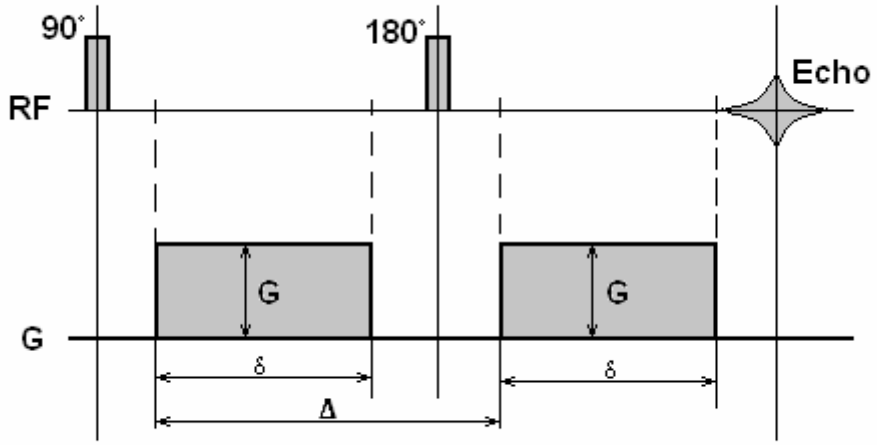

Fig. 4: *Pulse sequence of spin echo, with symmetrically placed diffusion gradients.*

4 CONCLUSION

For the observation of diffusion coefficient D it is necessary to do at least two measurements. In the first step, the pulse sequence without gradients is measured, to obtain the magnitude of signal not affected by diffusion. The pulse sequence with gradients is used for the next measurement (Fig. 4). Sequence parameters (δ,Δ,G) should be adjusted to reach a signal magnitude above the noise level. With suitably set sequence parameters a 10 % accuracy can be obtained.

The pulse sequence described in this paper is applicable to the measurement of diffusion coefficients in isotropic substances. Further research will be aimed at obtaining greater accuracy and versatility and also at the measuring being independent of *T1* & *T2* relaxation times.

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