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Laouès Guendouz, Sebastien Leclerc, Daniel Canet. NMR measurement of diffusion coefficients by radio-frequency gradients in the case of short relaxation times. *Journal of Magnetic Resonance*, 2024, 361, pp.107668. 10.1016/j.jmr.2024.107668 . hal-04534017

**HAL Id: hal-04534017**

<https://hal.univ-lorraine.fr/hal-04534017v1>

Submitted on 5 Apr 2024

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# NMR measurement of diffusion coefficients by radio-frequency gradients in the case of short relaxation times

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## Abstract

The measurement of translational diffusion coefficients by NMR generally makes use basically of two magnetic field gradient pulses separated by a so-called diffusion interval. The magnetic field gradient arises either from the static magnetic field (denoted by  $B_0$  used for polarizing the nuclear spins) or from the radio-frequency field (denoted by  $B_1$  used for inducing NMR transitions). The  $B_0$  method may be hampered by short effective transverse relaxation times ( $T_2^*$ ), by important gradient rise and fall times or by eddy currents. This does not occur with  $B_1$  gradients. Moreover, the effect of short transverse relaxation times during the gradient pulses is reduced by at least a factor of two. However, for  $B_1$  gradients, one might face with the limited volume in which the gradient is uniform and with the effect of short relaxation times which imply to reduce the various intervals in the diffusion experiment (this is as well true for the  $B_0$  method). Examples will be given for which the measurement of the diffusion coefficient by  $B_0$  gradients turned out to be impossible while a proper result was obtained with  $B_1$  gradients as far as a correction taking into account the limited volume is applied, together with a correction about the gradient calibration especially when dealing with samples containing paramagnetic species.

## Keywords

radio-frequency field gradients, diffusion measurements

## Introduction

For measuring the translational diffusion coefficient by NMR, one usually relies on magnetic field gradients. Gradients of the static magnetic field (dubbed  $B_0$  gradients) have been widely used notably since the seminal work of Stejskal and Tanner [1]. The idea is to modify the nuclear *precession* by a first gradient pulse which amounts to a spatial labeling or defocusing. This is followed by a so-called diffusion interval and a second gradient pulse (identical to the first one) leading to a refocusing process which is affected by translational diffusion, hence the possibility to measure the diffusion coefficient. In this pulsed field gradient spin echo (PFG SE) experiment, refocusing occurs thanks to a  $\pi$  hard pulse placed in the middle of the diffusion interval. It must be noticed that magnetization is transverse during the whole experiment and therefore subjected to the effective transverse relaxation time  $T_2^*$  which may be very short in some instances thus leading to an important signal loss. This inconvenient can be circumvented by the so-called simulated-echo (STE) experiment [2] with a  $\pi/2$  hard pulse after the first gradient pulse and prior to the second gradient pulse, along with the omission of the central  $\pi$  pulse. In that way, one is dealing only with longitudinal magnetization during the diffusion interval and consequently with the longitudinal relaxation time  $T_1$  generally much longer than  $T_2^*$ . This experiment is generally improved by bipolar gradient pulses [3] which avoid deleterious effects of magnetic susceptibility variations within a heterogeneous sample. Finally, another deleterious effect arises from eddy currents appearing after the gradient pulses which alter the NMR signal. This can be circumvented by the procedure LED [4] which consist of applying a  $\pi/2$  hard pulse after the second gradient pulse and an appropriate time interval prior to the acquisition of the NMR signal. Furthermore, rise and fall times of  $B_0$  gradients are not negligible. In principle, all these drawbacks could be lifted by the use of gradients of the radio-frequency field ( $B_1$  gradients).

Although homologous to the  $B_0$  gradient experiment, the  $B_1$  gradient experiment is much simpler [5,6]: two identical gradient pulses separated by a diffusion interval and followed by an observing  $\pi/2$  hard pulse for the NMR signal acquisition. The two  $B_1$  gradient pulses produce a *nutaton* process equivalent to precession viewed from the rotating frame), with defocusing due to the first one and refocusing depending on diffusion from the second one. Thanks to a simple two-step phase cycling (a  $180^\circ$  phase shift acting on the second gradient pulse), only longitudinal magnetization is concerned so that the  $B_1$  experiment could be considered as equivalent (though considerably simpler) to the  $B_0$  STE experiment. Indeed, it can be recalled that  $B_1$  gradient pulses enjoy negligibly small rise and fall times contrary to  $B_0$  gradient pulses which, for instance, prevent any acquisition of the NMR signal immediately after their application. Also,  $B_1$  gradients are totally immune to magnetic susceptibility variations within the sample under investigation and do not produce any eddy currents. Moreover, attenuation by transverse relaxation during the gradient pulses is much less severe with the  $B_1$  method. However, things are not so idyllic. First of all,  $B_1$  gradient amplitudes cannot be as intense as with  $B_0$  gradients. On the other hand, the volume inside which a  $B_1$  gradient is uniform is more limited than with  $B_0$  gradients. Finally, the diffusion experiment can be affected by short relaxation times and this is the major topic of the present study. As a matter of fact, it turns out that the  $B_0$  gradient method may become impracticable in the case of very short transverse relaxation times while  $B_1$  gradients can still fit the bill with nevertheless some adjustments required for these rather extreme situations.

### **The effect of very short transverse relaxation times with the $B_0$ gradient method**

The STE experiment with bipolar gradients is schematized in Fig. 1.

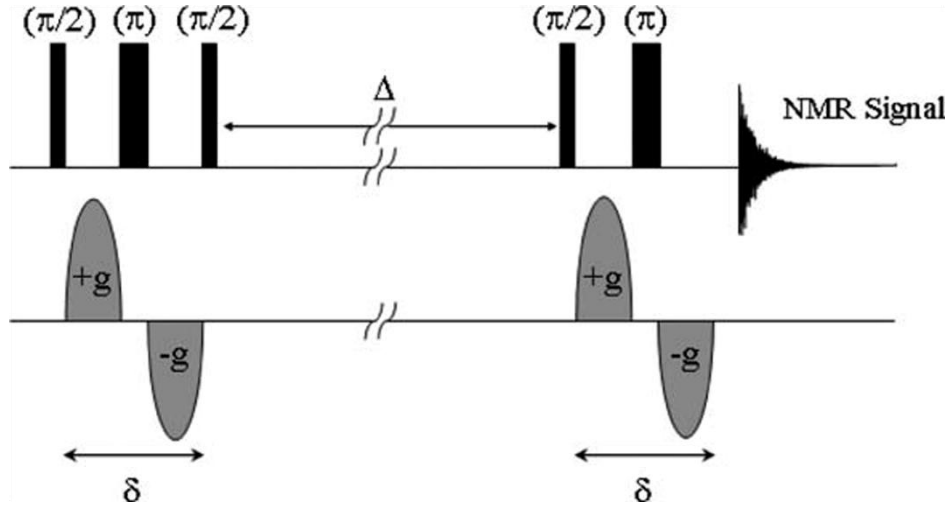


Fig. 1. Sketch of the sequence for measuring diffusion coefficients by  $B_0$  gradients according to the STE method described above.  $\delta$  is the duration of gradient application.  $\Delta$  is the diffusion interval. The gradient pulses are supposed to be shaped for minimizing the finite rise and fall times.

The amplitude of the NMR signal is given by Eq. (1) below.

$$S(\delta, \Delta) \propto \exp\left(-\frac{2\delta}{T_2^*}\right) \exp\left(-\frac{\Delta}{T_1}\right) \exp\left[-\gamma^2 4g^2 \delta^2 D(\Delta + 2\delta/3)\right] \quad (1)$$

$\gamma$  is the gyromagnetic ratio,  $D$  the diffusion coefficient,  $T_1$  the longitudinal relaxation time and  $T_2^*$  the effective transverse relaxation time with  $\frac{1}{T_2^*} = \frac{1}{T_2} + \frac{1}{T_2'}$  (on-resonance conditions),  $T_2$  being the true transverse relaxation time and  $T_2'$  accounting for the residual inhomogeneity of  $B_0$ . When  $T_2$  and  $T_2'$  become very short, the NMR signal can be severely attenuated and this the major drawback of the  $B_0$  gradient method.

### The effect of very short relaxation times with the $B_1$ gradient method

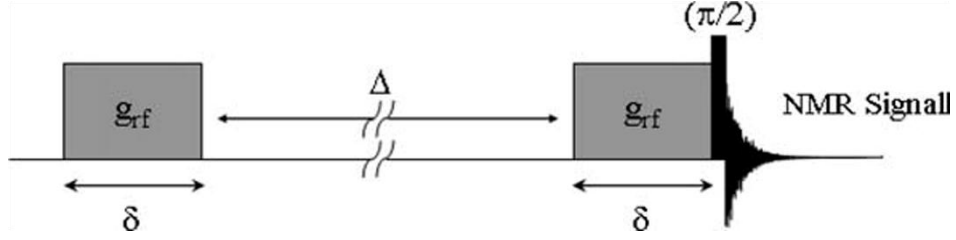


Fig. 2. Sketch of the sequence for measuring diffusion coefficients by  $B_1$  gradients. See Fig. 1 for the meaning of the various symbols.  $g_{rf}$  stands for the  $B_1$  gradient pulse. The second gradient pulse is subjected to the phase cycling ( $0^\circ, 180^\circ$ ) for retaining only longitudinal magnetization.

The experiment using  $B_1$  gradients is shown in Fig. 2. The first gradient pulse produces a nutation (rotation around the rf field in the so-called rotating frame comparable to the precession around the  $B_0$  field in the normal frame) with spatial labeling, that is a defocusing process. The second gradient pulse produces a refocusing process depending on translational diffusion which took place during the so-called diffusion interval  $\Delta$ . If everything goes well, the NMR signal is expressed as

$$S(\delta, \Delta) \propto \exp\left(-\frac{2\delta}{T_{2\rho}}\right) \exp\left(-\frac{\Delta}{T_1}\right) \exp[-\gamma^2 g_{rf}^2 \delta^2 D(\Delta + 2\delta/3)] = A \exp[-\gamma^2 g_{rf}^2 \delta^2 D(\Delta + 2\delta/3)]$$

(2)

with the same notations as in Eq. (1), except one has  $\frac{1}{T_{2\rho}} = \frac{1}{2} \left( \frac{1}{T_1} + \frac{1}{T_2} \right)$ . *This is the major difference with the  $B_0$  gradient method.* First of all,  $T_{2\rho}$  is totally independent of the  $B_0$  inhomogeneity. Secondly, if  $T_1 \gg T_2$  (as this is often the case in complex systems),  $T_{2\rho} \cong 2T_2$  meaning that *the attenuation due to transverse relaxation is much less important than with  $B_0$  gradients* ( $e^{-\delta/2T_2} \gg e^{-\delta/T_2^*}$ ). This feature represents a considerable advantage of  $B_1$  gradients (see below).

The experimental set up consists of a coil assembly delivering a uniform  $B_1$  gradient along the NMR sample tube (that is vertically) and of an additional coil delivering a homogeneous rf field

used for hard pulses and for the NMR signal detection. The gradient coil assembly and the additional transmit-receive coil are electrically independent and require two independent transmitters.

### **Particularities of the $B_1$ gradient diffusion experiment**

By fitting data obtained with different values of  $g_{rf}$ , one can deduce the value of  $D$ , provided that  $g_{rf}$  has been properly calibrated. There stands one of the problems we shall be dealing with. The first idea is to refer to a sample (*e.g.* pure water) for which  $D$  and  $T_{2\rho}$  are perfectly known and to determine  $g_{rf}$  for each experimental setting (in terms of rf gradient) by varying  $\delta$ .

Things are not so easy. We must first consider a simple nutation experiment. Let  $\omega_1 = \gamma B_1$ , where  $B_1$  is the amplitude of the radio-frequency field. Let us further define  $R_D$  as  $R_D = \frac{1}{2}(\frac{1}{T_2} - \frac{1}{T_1})$ . It has been shown [7] that if  $\omega_1 > R_D$ , the nutation phenomenon consists of an oscillation at the angular frequency

$$\omega_1^{eff} = \sqrt{\omega_1^2 - R_D^2} \quad (3)$$

By contrast, when  $\omega_1 < R_D$ , nutation no longer occurs and the concerned longitudinal magnetization no longer oscillates but is simply reduced by relaxation during the gradient pulses and the diffusion interval. However, it turns out that, in practice,  $\omega_1$  is much larger than  $R_D$ . Consequently, these effects on the nutation angular frequency can generally be ignored.

Let us now look at the rf profile produced by a device generating a rf gradient and shown in Fig. 3 [8]

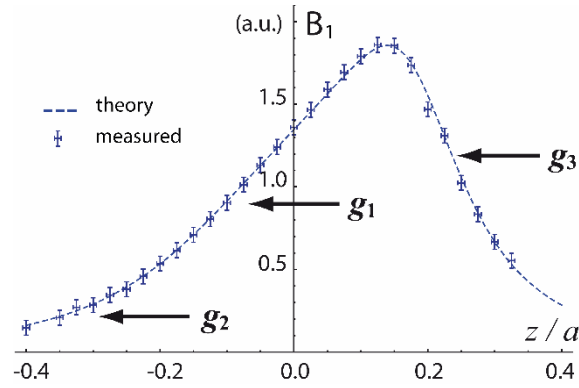


Fig. 3. A typical radiofrequency field profile measured in free space by a pick-up coil for the device of ref. [8].  $a$  is the radius of the major coil in the coil assembly delivering the  $B_1$  gradient [8].  $g_1$  is the operative uniform gradient. The sample may experience secondary (possibly unwanted) gradients  $g_2$  and  $g_3$ .

What is important is the  $B_1$  field acting on the *whole* sample. Ideally, the sample would be positioned so that, for each elementary slice located at abscissa  $z$ , it would experience a rf field equal to  $g_1 z$ . In practice, this may be not always the case and a part of the sample may be located in the zones labeled as  $g_2$  and  $g_3$  in Fig. 3, or in peripheral zones where the  $B_1$  field is smaller than expected.

Suppose now that for the sample used for calibrating the gradient (*i.e.* a sample completely filled with pure water as it has been the case in this study), because of long relaxation times, relatively large values of  $\delta$  and  $\Delta$  can be used. In spite of that, the estimated value for the gradient  $g_1$  (obtained from the experiment performed by varying  $\delta$  as described above) may be slightly in error just because the evolution of magnetization corresponding to the zone  $g_2$  (and possibly  $g_3$ ) is part of the diffusion curve. This value will be denoted  $g^{cal}$  and, as shown in Fig. 4, leads to a perfect value of the diffusion coefficient for the normal experiment performed by incrementing the gradient.



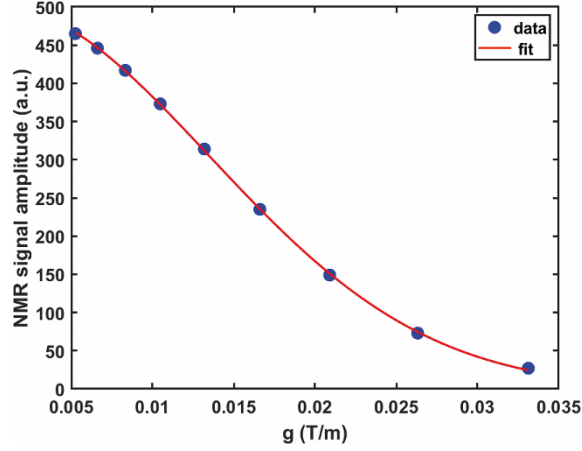


Fig. 4. Dots: amplitude of the NMR signal obtained by the sequence of figure 2 as a function of incremented gradient values ( $g^{cal}$ ) for a sample completely filled with pure water ( $\delta=6$  ms,  $\Delta=500$  ms). Continuous curve: fit according to Eq. (2) leading to the expected value of  $2.1 \cdot 10^{-9} \text{ m}^2 \text{ s}^{-1}$  for the diffusion coefficient.

It can be noted that, for experimental conditions of Fig. 4, we are dealing with the sample used for calibration purpose. It is therefore not surprising that everything goes well.

In a general way, provided that the sample experiences a uniform gradient, the diffusion curve can be expressed as

$$y = A \exp[-K (g^{eff})^2] \quad (4)$$

$A$  is the global amplitude including the instrumental receptivity and  $\exp(-\frac{2\delta}{T_{2\rho}})\exp(-\frac{\Delta}{T_1})$  (see Eq.

(2)). Again, from Eq. (2), one has

$$K = \gamma^2 \delta^2 D \Delta \quad (5)$$

In order to get some insight into the diffusion curve of Fig. 4, which has been obtained for a sample completely filled, let us suppose that the two zones  $g_1$  and  $g_2$  are involved so that

$$y = A_1 \exp[-K(g_1)^2] + A_2 \exp[-K(g_2)^2] \quad (6)$$

where  $A_1$  and  $A_2$  include the magnetizations experiencing the zones  $g_1$  and  $g_2$ , respectively.

Expanding to first order the exponential functions, we obtain

$$y = A_1 + A_2 - K(A_1 g_1^2 + A_2 g_2^2) \quad (7)$$

Because  $A_2 g_2^2$  is very likely to be much smaller than  $A_1 g_1^2$  (see for instance Fig 3), we can write

$$y = (A_1 + A_2) \left(1 - K \frac{A_1}{A_1 + A_2} g_1^2\right) \quad (8)$$

Two important conclusions can be drawn from Eq. (8). First, as observed experimentally, the diffusion curve is a mono-exponential. Secondly, the effective gradient (used as  $g^{cal}$  in the following) is not  $g_1$  but smaller than  $g_1$ :

$$g^{cal} = \sqrt{\frac{A_1}{A_1 + A_2}} g_1 \quad (9)$$

Now, for another sample,  $g^{eff}$  may be slightly different from  $g^{cal}$  depending on the magnetic susceptibility of this sample (if it contains paramagnetic species which are known to increase the magnetic permeability), from the way it has been filled, and from its positioning in the gradient assembly. So that we can write for the  $i^{\text{th}}$  data point of the diffusion curve

$$g_i^{eff} = g_i^{cal} + \varepsilon \quad (10)$$

and

$$\exp[-K(g_i^{eff})^2] = \exp[-K(g_i^{cal})^2] \exp(-2K\varepsilon g_i^{cal}) \quad (11)$$

where  $(g_i^{eff})^2$ , as a function of  $\varepsilon$ , has been limited to first order:  $(g_i^{eff})^2 \approx (g_i^{cal})^2 + 2\varepsilon g_i^{cal}$ .

Now, expanding  $\exp(-2K\varepsilon g_i^{cal})$  still to first order;  $\exp(-2K\varepsilon g_i^{cal}) \approx 1 - 2K\varepsilon g_i^{cal}$ , we obtain

$$y_i^{exp} = A(1 - k g_i^{cal}) \exp[-K(g_i^{cal})^2] \quad (12)$$

where  $k = 2K\epsilon$  which must be determined from experimental data together with  $A$  and  $D$  (through  $K$ ). It can be noticed that Eq. (12) is the general expression which must imperatively be used for treating experimental diffusion data obtained by the  $B_1$  gradient methodology. This is especially the case when  $\delta$  and  $\Delta$  are short (due to small relaxation times) making the value of  $g_i^{eff}$  rather critical.

## Results

Test experiments were carried out with samples for which  $B_0$  gradients totally failed (at least with gradients available with our spectrometer:  $\leq 20$  G/cm). We were dealing with a water solution which contains *paramagnetic* species, *i.e.* 4mM of  $MnCl_2$ , for lowering relaxation times and providing a  $T_1$  value of 50 ms and a  $T_2$  value of 3 ms. This short value of  $T_2$  explains the failure of  $B_0$  gradient experiments for which the NMR signal is so deteriorated that any diffusion measurement turns out to be impossible. By contrast, the  $B_1$  method becomes feasible. The experiments were performed with gradient pulses of duration  $\delta = 2$  ms and a diffusion interval  $\Delta = 50$  ms. Eight gradient values ranging from 0.5 G/cm up to 3.3 G/cm were used for obtaining a diffusion curve compatible with the usual value of the water diffusion coefficient.

The first sample was filled and positioned so that it tentatively occupies the zone  $g_1$  where the gradient is supposed to be uniform. It turns out that a classical data treatment does not provide a correct value for the water diffusion coefficient (Fig. 5). Moreover, data points at low values of the gradient appear erratic. This is presumably due to interfaces in this incompletely filled sample tube. If these interfaces are located *within* the detection coil, it is well known that they generate small gradients of any magnetic field. When these parasitic gradients are not negligible with

respect to an applied gradient, they entail necessary distortions in the experimental result. We can then decide to disregard these corrupted data points and to concentrate on the last four data points *and to process data with corrected gradient values according to Eq. (12)*. This is shown in Fig. 6 and, indeed, a correct value for the diffusion coefficient is regained.

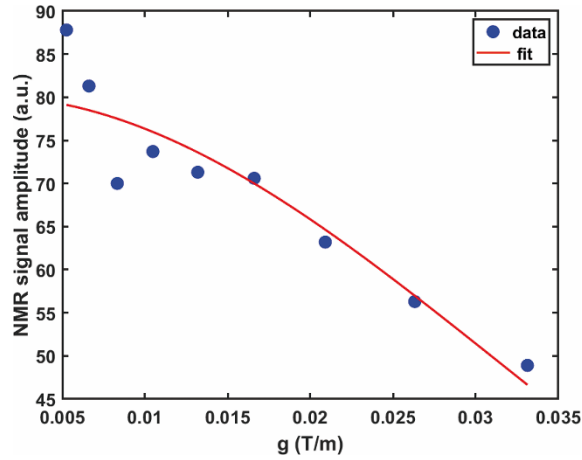


Fig. 5. Dots: amplitude of the NMR signal of the test sample described in the text (filled and positioned for experiencing only the zone where the gradient is uniform) obtained by the sequence of Fig. 2 as a function of incremented gradient values ( $g^{cal}$ ). Duration of gradient pulses: 2 ms; duration of the diffusion interval: 50 ms. Continuous curve: fit according to Eq. (2) leading to an unrealistic value of  $34 \cdot 10^{-9} \text{ m}^2\text{s}^{-1}$  for the diffusion coefficient (a fit according to Eq. (8) leads to a more aberrant result).

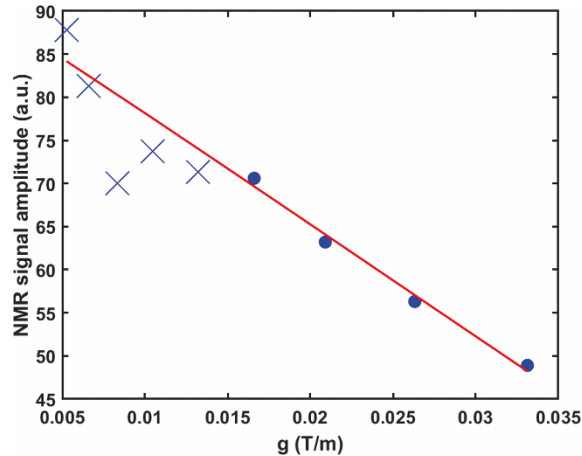


Fig. 6. Same data as in Fig. 5 but with the first five points suppressed and a fit according to Eq. (12) yielding  $k=13.6$  and  $D=2.0 \cdot 10^{-9} \text{ m}^2\text{s}^{-1}$ .

The next step was to use a sample completely filled with same solution (involving short relaxation times). Indeed, as shown in Fig. 7, the diffusion curve is clean (without erratic data points at low gradient values).

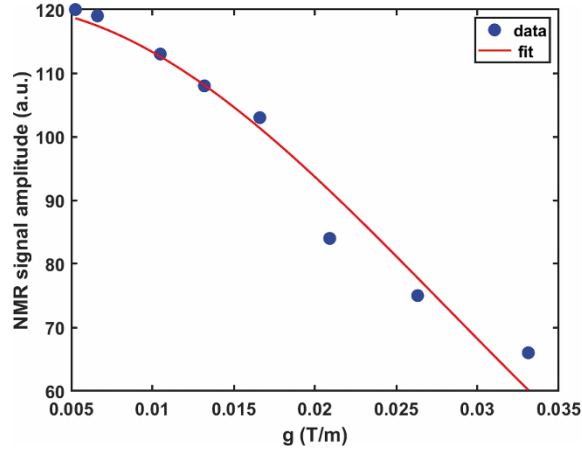


Fig. 7. Dots: amplitude of the NMR signal of a completely filled sample tube with the same solution as in Fig. 5 obtained by the sequence of Fig. 2 as a function of incremented gradient values ( $g^{cal}$ ). Same experimental parameters as in Fig. 5. Continuous curve: fit according to Eq. (2) leading to an unrealistic value of  $44 \cdot 10^{-9} \text{ m}^2\text{s}^{-1}$  for the diffusion coefficient.

Not surprisingly, the conventional data treatment (Eq. (2)) produces a totally wrong result for the diffusion coefficient (Fig. 7). Hence, we must rely to the corrected gradient values given by Eq. (12). However, a careful examination of experimental data reveals that the diffusion curve can be decomposed into two regimes. The first regime which corresponds to the lowest gradient values, exhibits an upward shift. This can be ascribed to a zone (presumably  $g_2$ ) experienced by this completely filled sample where the gradient is especially weak. As we are dealing with short  $\delta$  and  $\Delta$  values (because of short relaxation times), the quantity  $\exp[-\gamma^2 \delta^2 D \Delta (g_{rf})^2]$  remains very close to 1 and therefore does not contribute to the diffusion curve. As this shift is easily determined from experimental data, it can be eliminated and the usual data processing with gradient corrections (Eq. (12)) can be applied. Thereafter, this processing is again applied to the

data points of the second part of the diffusion curve, with possibly a different value for  $k$ . This procedure is validated by the excellent agreement between experimental data and the recalculated curve as shown in Fig. 8. In addition, and this is mostly important, a quite correct value of the diffusion coefficient is obtained through the global application of this procedure.

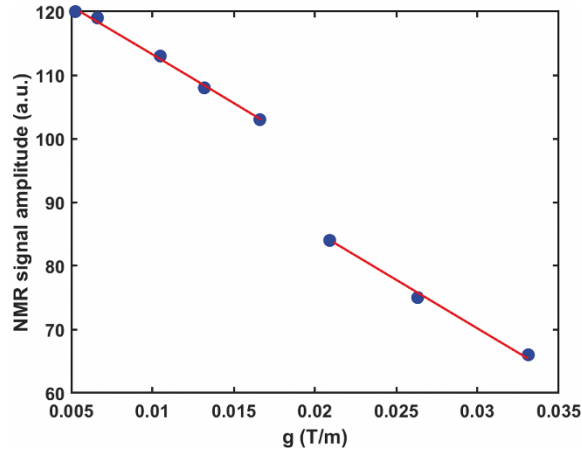


Fig. 8. Dots: same experimental data as in Fig. 7. Continuous curve: fit according to the procedure described in the text.  $k = 12.69$  for the regime of low gradient values and  $12.44$  for the regime of high gradient values. This global fit leads to the expected diffusion coefficient of  $2.2 \cdot 10^{-9} \text{ m}^2\text{s}^{-1}$ .

## Experimental

Experiments have been performed at 100 MHz in a horizontal magnet (Bruker Biospec) possessing a large aperture for accommodating the device described in ref. [8]. The sample tube is placed vertically, perpendicular to the  $B_0$  field. The assembly for generating the  $B_1$  gradient is made of three horizontal coaxial coils in series of diameter and position which have been optimized for delivering a uniform gradient of maximum value of 0.038 T/m for a transmitter power of 150 W [8]. The transmit-receive coil is of saddle shape type and surrounds the sample. The duration of the  $90^\circ$  hard pulse is 20  $\mu\text{s}$ . The pulse program activates separately the two

transmitters for gradient pulses or for hard pulses. Data treatment has been performed by least-squares in dedicated MATLAB computer programs.

## **Conclusion**

When dealing with short relaxation times in diffusion experiments, the duration of gradient pulses and of the diffusion interval must be reduced. The shortness of gradient pulses may prevent the use of  $B_0$  gradient technology. This may not be the case with  $B_1$  gradient technology which can accommodate very short gradient pulses and which affords a much simpler sequence. However, due to the proximity between the sample and the coils delivering the  $B_1$  gradient, the value of the latter may be slightly influenced by the configuration and the nature of the sample. Indeed, if the sample contains paramagnetic species, this entails necessarily an alteration of the  $B_1$  field due to the increase of the magnetic permeability. Hence, if the gradient has been calibrated with a given sample, this calibration may not strictly apply to the sample under investigation. This is especially a problem for short gradient pulses, mandatory when dealing with short relaxation times. The main objective of the present study was to circumvent this problem so that an appropriate diffusion coefficient could be deduced from experimental data. Fortunately, this can be successfully achieved by introducing an additional parameter for defining the true value of the gradient with respect to the value obtained from the calibration process. This parameter has been shown to be easily obtained through an extended data treatment which leads finally to the proper diffusion coefficient. In summary, it has been demonstrated that when

diffusion measurements turn out to be impossible by  $B_0$  gradients, the alternative by  $B_1$  gradients is feasible provided that an adapted data treatment is carried out.



## REFERENCES

- [1] E.O. Stejskal, J.E. Tanner, spin diffusion measurements: spin echoes in the presence of a time-dependent field gradient, *J. Chem. Phys.* 42 (1965) 288-292.
- [2] J.E. Tanner, Use of the stimulated echo in NMR diffusion studies, *J. Chem. Phys.* 52 (1970) 2523-2526.
- [3] R.M. Cotts, M.J.R. Hoch, T. Sun, J.T. Marker, Pulsed field gradient simulated echo methods for improved NMR diffusion measurements in heterogeneous systems, *J. Magn. Reson.* 83 (1989) 252-266.
- [4] S.J. Gibbs, C.S. Johnson Jr., APFG NMR experiment for accurate diffusion and flow studies in the presence of eddy currents, *J. Magn. Reson.* 93 (1991) 395-402.
- [5] D. Canet, B. Diter, A. Belmajdoub, J. Brondeau, J.C. Boubel, K. Elbayed, Self-diffusion measurements using a radio-frequency field gradient, *J. Magn. Reson.* 81 (1989) 1-12.
- [6] D. Canet, Radiofrequency field gradient experiments, *Prog. Nucl. Magn. Reson. Spectrosc.* 30 (1997) 101-135.
- [7] M. Ferrari, C. Moyne, D. Canet, Measurements of short transverse relaxation times by pseudo-echo nutation experiments, *J. Magn. Reson.* 292 (2018) 8-15.
- [8] L. Guendouz, S. Leclerc, A. Retournard, P.-L. Marande, D. Canet, Design of a three-loop asymmetric coil producing a homogeneous radiofrequency  $B_1$  field gradient along the axis of a vertical sample tube, *J. Magn. Reson.* 347 (2023) 107362.

## Declaration of Competing Interest

None.

**Funding:** This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Graphical abstract

