



# An improved approach to calibrating high magnetic field gradients for pulsed field gradient experiments

Nirbhay N. Yadav, Allan M. Torres, William S. Price \*

Nanoscale Organisation and Dynamics Group, College of Health and Science, University of Western Sydney, Locked Bag 1797, Penrith South DC, NSW 1797, Australia

## ARTICLE INFO

### Article history:

Received 18 April 2008

Revised 21 May 2008

Available online 24 May 2008

### Keywords:

Diffusion

Gradient calibration

Pulsed gradient spin-echo

## ABSTRACT

Probes capable of generating short high intensity pulsed magnetic field gradients are commonly used in diffusion studies of systems with very short  $T_2$ . Traditional methods of calibrating magnetic field gradients present unique challenges at ultrahigh field strengths and are often inapplicable. Currently the most accurate method of determining magnetic gradient strength is to use the known diffusion coefficient of a standard sample and determine gradient strength from the echo attenuation plot of a diffusion experiment, however, there are problems with finding suitable standards for high intensity gradients. Here, we show that molecules containing at least two receptive nuclei (i.e. one with high and one with low gyromagnetic ratios) are excellent systems for calibrating high intensity gradients.

© 2008 Elsevier Inc. All rights reserved.

## 1. Introduction

Pulsed gradient spin-echo (PGSE) NMR diffusion measurements is an indispensable characterisation tool in many fields of science ranging from nanoscience [1] to food science [2] and to petroleum exploration [3]. Translational diffusion measurements are carried out by varying the magnetic gradient amplitude ( $g$ ), gradient duration ( $\delta$ ), or diffusion time ( $\Delta$ ) then studying the attenuation of the spin-echo signal [4]. In systems with short  $T_2$  (e.g. restricted diffusion measurements in porous materials) the extent to which  $\delta$ , and  $\Delta$  can be extended is limited therefore there is a need for probes capable of applying short, high amplitude pulses ( $> 10 \text{ T m}^{-1}$ ). Such probes are becoming common and, in recent years, probes capable of applying ultra high intensity gradient pulses have also been developed [5–7]. The calibration of high intensity gradients does, however, present unique challenges which can prevent accurate diffusion measurements. Importantly, the ultimate accuracy of a diffusion measurement is determined by the accuracy of the gradient calibration.

Many problems, which are insignificant at low field strengths, can arise when switching high intensity magnetic field gradients. These include eddy currents generated in conducting surfaces surrounding the gradient coil [8], mismatched gradient pulses [9], coil vibration [9,10], and gradient uniformity across the length of the sample [11]. Here, we are mainly concerned with the calibration of high intensity magnetic field gradients and ensuring the effective gradient output is a linear function of the input parameter con-

trolling the current amplitude. Gradient calibrations carried out at low gradient amplitudes cannot be extrapolated to higher gradient amplitudes, especially for very short pulses because eddy currents, coil resistance, and coil vibration can change with gradient strength. Below we discuss the most common gradient calibration procedures and highlight challenges which are present at high magnetic gradient field strengths.

First, the most fundamental method for the determination of gradient strengths is to do theoretical calculations based on gradient coil dimensions, geometry, number of turns of wire, and applied current [12]. However, this method is inaccurate because it does not account for interactions with nearby metal in the probe and non-ideal gradient pulse generation. Second, the echo shape or line width of the Fourier transformed spectrum of a sample of known geometry can be used to calculate the gradient strength [13,14]. The presence of a read gradient will result in a spatial dependence of the resonance frequency therefore if the sample length perpendicular to the gradient ( $l$ ) is known, the linewidth ( $\nu$ ) (Hz) can be measured and used to determine the gradient strength ( $g$ ) from

$$\nu = \frac{\gamma g l}{2\pi} \quad (1)$$

where  $\gamma$  is the gyromagnetic ratio. This technique can be performed without knowledge of the diffusion coefficient and can provide an error of less than 5% if the sample dimensions are not temperature dependant. This type of “projection” analysis (i.e. 1D imaging) can additionally be used for checking the constancy of the gradient over a range of temperatures and over the length of the sample. Analogous to this method, the gradient can also be calibrated by relating precision displacements of the sample to the subsequent frequency

\* Corresponding author. Fax: +61 2 4620 3025.

E-mail address: [w.price@uws.edu.au](mailto:w.price@uws.edu.au) (W.S. Price).

shift of the NMR spectrum [15]. An advantage of using the frequency shift over the line shape is that the position in the frequency space is clearly defined whereas when using the line shape, the edges of the projection can become quite arbitrary, especially at high gradient strengths. Major problems which arise when using the echo shape, line width, or frequency shift for calibrating high intensity pulses are that large receiver bandwidths are required at even modest gradient strengths and the gradient broadened spectrum makes it difficult to obtain adequate signal-to-noise ( $S/N$ ). By restricting the length of the sample ( $l$ ) or using slice selective pulses, one can alleviate problems with spectrometer bandwidth, however, restrictions due to  $S/N$  become more significant.

Third, gradient strength can be determined from the echo shape by intentionally mismatching the duration of the gradient pulses [16] although this technique is still limited by the extremely short echo time at high gradient strengths. Wright et al. [7] recently developed a two stage calibration procedure for high intensity pulsed field gradients where the gradient is calibrated at low field strengths ( $< 4 \text{ T m}^{-1}$  in this case) then based on this value, used an echo based technique to calibrate a high intensity pulse of shorter duration. This technique is useful because a standard sample with a known diffusion coefficient is not required (if the low amplitude pulse is calibrated from the line width). The two pulses of opposite polarity are adjacent to each other, to reduce diffusion effects, mean that eddy current artefacts may be present. Eddy current problems are exacerbated because gradient pulses are of different amplitude and quantified from the current amplifier output which may differ in shape when compared to the output of the gradient coils [17].

Finally, if a “standard” sample with a “known” diffusion coefficient is available, regression analysis can be used to determine gradient strength from an echo attenuation plot. This is currently the most accurate way of calibrating magnetic field gradients (error  $< 1\%$ ) and is preferred because it includes non-ideal behaviour (e.g. rise and fall times, droop or residual gradients) if the same experimental parameters are used (i.e. pulse shape, delays, pulse length, gradient strengths, etc.) in subsequent experiments. Comprehensive lists of known diffusion coefficients of relatively fast moving molecules at different temperatures are given in many references [18–22]. Still the calibration of very high gradient amplitudes present problems such as the difficulty in finding suitable diffusion standards. Standards with very small, and more importantly reproducible, diffusion coefficients are hard to find. For example glycerol, which has often been used, has a diffusion coefficient which is greatly affected by its water content as well as a highly temperature dependant diffusion coefficient and  $T_2$  [23]. Polymer standards also present many problems because they are synthetic and in general polydisperse. Therefore, ensuring different batches of the same polymer are identical and have the same polydispersity is a significant problem. Polymers in general have to be dissolved in organic solvents, which, compared to water have greater propensity for convection. Also for polydisperse samples, a change in the diffusion measuring time ( $\Delta$ ) may mean a different distribution is observed thus giving a different diffusion coefficient.

Presently, the most reliable diffusion standards have a diffusion coefficient of the order of  $10^{-9} \text{ m}^2 \text{ s}^{-1}$ . Therefore, a gradient of the order of  $0.05\text{--}0.10 \text{ T m}^{-1}$  is all that is required to completely suppress the  $^1\text{H}$  resonance and thus limiting calibration of higher field strengths. A multinuclear probe capable of measuring nuclei with lower  $\gamma$  (i.e.  $^2\text{H}$ ) would allow for the calibration of a much larger range of gradient amplitudes because low  $\gamma$  resonances are still visible at much higher magnetic field strengths. A molecule labelled with two NMR active nuclei also presents the opportunity to remove a significant variable in calibrating probes at high and low gradient field strengths because a single sample can be used. The diffusion of  $^2\text{H}_2\text{O}$  is well-characterised nevertheless it is difficult to find instances where low  $\gamma$  nuclei have been used to calibrate

a high intensity gradient probe. Here, we show that observing low  $\gamma$  nuclei is an excellent method for the calibration of very high gradient strengths, and also presents the opportunity to test a range of gradient strengths from a single sample thus ensuring that the gradient output is a linear function of the input parameter controlling current amplitude. For comparison, gradient strengths were also determined using the widely used projection technique.

## 2. Materials and methods

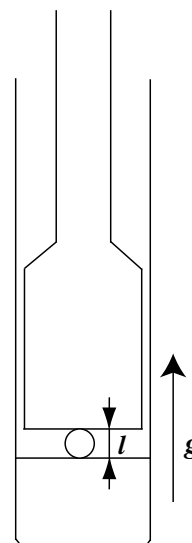
Samples for diffusion measurements were prepared by placing  $^2\text{H}_2\text{O}$  in susceptibility matched microtubes (Shigemi, Tokyo) and the sample height restricted to approximately 10 mm to ensure it lay within the constant region of the applied gradient. The sample to be used in the projection technique was prepared by placing  $\text{H}_2\text{O}$  in the cavity between the base and plunger of a susceptibility matched tube (see Fig. 1). The sample height was precisely set by wedging a small glass capillary with diameter 0.51 mm between the base and the plunger. The wedge was placed in the centre of the tube to reduce background gradient errors which might arise when measuring the line width.

$^1\text{H}$  and  $^2\text{H}$  NMR experiments were performed at 298 K on a Bruker Avance 500 wide bore spectrometer equipped with a Diff30 gradient probe (producing approx.  $0.3 \text{ T m}^{-1} \text{ A}^{-1}$ ) with a single (i.e.  $z$ ) shielded gradient coil connected to a GREAT60 current amplifier capable of generating current pulses of 60 A amplitude.  $^1\text{H}$  measurements were performed at 500.1 MHz whilst  $^2\text{H}$  measurements were performed at 76.77 MHz. The sample temperature was calibrated using the temperature dependant chemical shift of methanol.

The Hahn spin-echo pulse sequence containing “rectangular” gradient pulses in each  $\tau$  period was used for the translational diffusion experiments. For a single diffusing species the normalised echo attenuation,  $E$ , is related to the experimental parameters and self-diffusion coefficient,  $D$ , by Stejskal and Tanner [24]

$$E = \exp\left(-D\gamma^2 g^2 \delta^2 \left(\Delta - \frac{\delta}{3}\right)\right) \quad (2)$$

where  $\Delta$  is the separation between the leading edges of the gradient pulses. Nonlinear regression of Eq. (2) onto the spin-echo attenua-



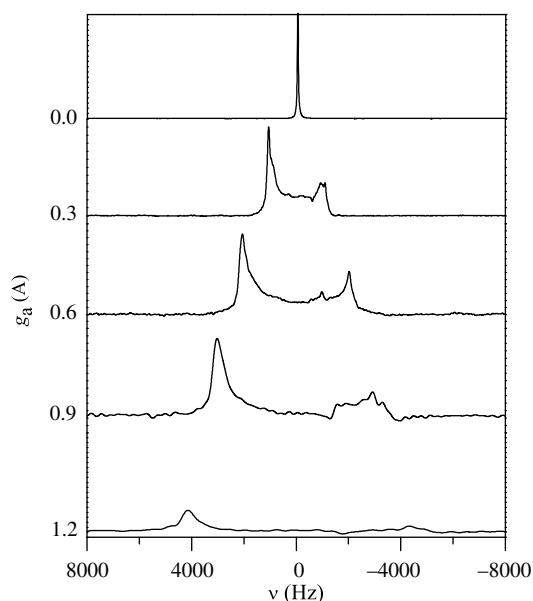
**Fig. 1.** Water filled cavity in a susceptibility matched tube used for the projection method of calibrating magnetic gradient strengths. The length of the cavity  $l$  was precisely determined by placing a piece of glass capillary in the centre of the cavity. The diameter of the capillary was determined to be 0.51 mm using a micrometer screw gauge.

tion data, based on the integrals of the  $^1\text{H}$  and  $^2\text{H}$  resonances, was performed to determine  $g$  and associated error margins in Origin ver. 8.0 (Microcal, MA), which is based on the Levenberg–Marquardt algorithm. Experimental parameters used in the  $^1\text{H}$  and  $^2\text{H}$  experiments were  $\Delta = 20$  ms and  $\delta = 0.8$  ms whilst the gradient input parameter controlling current amplitude,  $g_a$ , was incremented in the range of 0–6 A for  $^1\text{H}$  experiments and 0–55 A for  $^2\text{H}$  experiments.  $D$  values used in the regression analysis were  $1.90 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$  for the diffusion coefficient of residual  $\text{HO}^2\text{H}$  in  $^2\text{H}_2\text{O}$  [18] and  $1.87 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$  for  $^2\text{H}_2\text{O}$  [25]. Eight scans were averaged for each value of  $g_a$  with the delay between subsequent scans in the PGSE was 10 s for the  $^2\text{H}$  measurements. This value was made much longer than required for complete longitudinal relaxation of the  $^2\text{H}$  nuclei to avoid problems with coil overheating. The recycle delay for the  $^1\text{H}$  measurements was 25 s (i.e.  $5 \times T_1$ ). The projection technique was carried out by using a single scan for  $g_a$  values ranging from 0 to 1.2 A.

### 3. Results and discussion

Gradient strengths were unable to be determined from the 0.9 and 1.2 A  $z$ -axis projections in Fig. 2 because of poor S/N. The 0.6 A projection (which had adequate S/N) gave a  $g$  value of  $0.175 \pm 0.006 \text{ T m}^{-1}$  when using Eq. (1) which when extrapolated to 60 A (i.e. maximum current amplitude) gives a  $g$  value of  $17.5 \pm 0.6 \text{ T m}^{-1}$ . Using the same sample and a larger spectrometer bandwidth, it is theoretically possible to directly determine gradient strengths up to  $20 \text{ T m}^{-1}$  but as seen in Fig. 2, the S/N deteriorates to the point where the technique is unusable beyond a fraction of a  $\text{T m}^{-1}$ . Using a longer sample would mean a larger volume and hence improved signal-to-noise but this would limit the range of gradient strengths which can be calibrated.

Another possibility when using projection methods is to use the resonance of a low  $\gamma$  nuclei. A broader range of gradient strengths can theoretically be observed, however, the critical flaw with observing low  $\gamma$  nuclei is that they are significantly less sensitive. Any advantage which can be gained from using low  $\gamma$  nuclei would be significantly outweighed by a reduction in signal-to-noise.

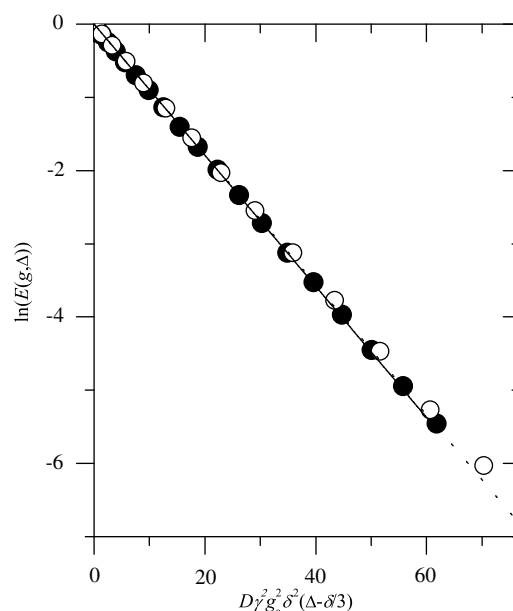


**Fig. 2.**  $z$ -axis projection of  $\text{H}_2\text{O}$  in the cavity of a susceptibility matched tube (see Fig. 1). The scan acquired during a gradient using 0.6 A gave a maximum gradient strength  $g = 17.5 \pm 0.6 \text{ T m}^{-1}$ . We tried to centre the 0.5 mm sample to the centre of the gradient coils, however, the lack of symmetry suggests the samples were not perfectly centred. Subsequently, the frequency was manually set to zero at the centre of each projection.

The results of the diffusion experiment on  $^2\text{H}_2\text{O}$  are shown in Fig. 3. Maximum gradient strength determined from the  $^1\text{H}$  (low current amplitudes) and  $^2\text{H}$  (high current amplitudes) resonances agree within experimental uncertainty. Maximum gradient strengths determined from high and low values of  $g_a$  were verified by further diffusion experiments at intermediate values of  $g_a$  (whilst  $\Delta$  was varied) and all values for  $g$  agree with Fig. 3. This indicates the effective gradient output is a linear function of the input parameter controlling the current amplitude. It is important to use both the  $^1\text{H}$  and  $^2\text{H}$  resonances for verifying the linearity of the gradient output with the input parameter because the spin-echo signal must attenuate at least an order of magnitude in order to carry out accurate diffusion experiments. To achieve the same amount of attenuation at high and low field strengths by only varying  $\Delta$  or  $\delta$  may introduce eddy current artefacts.

Despite all  $g$  values agreeing within experimental uncertainty, the error determined from the diffusion experiments is significantly less than that obtained from the projection technique (see Table 1). So if a probe is capable of observing multiple nuclei, considerable advantages are gained by carrying out diffusion experiments on a well studied sample (with an accepted value for  $D$ ) for calibrating high intensity gradients. Furthermore, a sample containing NMR sensitive nuclei with a broad range of  $\gamma$  values allowed the determination of  $g$  from high and low current amplitudes. The opportunity to calibrate a range of gradient strengths with a single sample is very convenient and removes a major source of errors; also dilution problems are not an issue. Another major advantage of calibrating gradient strengths from a standard  $D$  value is that if more accurate diffusion coefficients are determined in the future, updating the gradient strength would be trivial.

A sample of pure  $^2\text{H}_2\text{O}$ , as used here, would still be suitable for calibrating higher strength gradient pulses ( $> 25 \text{ T m}^{-1}$ ) if smaller values of  $\Delta$  and  $\delta$  are used. The use of nuclei with lower  $\gamma$  such as  $^{15}\text{N}$  is also currently feasible (i.e.  $^2\text{H}$  and  $^{15}\text{N}$  labelled dimethylformamide) thus allowing for the calibration of higher magnetic



**Fig. 3.** PGSE attenuation plots of the  $^1\text{H}$  (open dots) and  $^2\text{H}$  (closed dots) resonances in 99.9%  $^2\text{H}_2\text{O}$ . For the  $^1\text{H}$  resonance  $D = 1.90 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ ,  $\gamma = \gamma_{^1\text{H}}$  and  $g_a$  incremented from 0 to 6 A. For the  $^2\text{H}$  resonance  $D = 1.87 \times 10^{-9} \text{ m}^2 \text{ s}^{-1}$ ,  $\gamma = \gamma_{^2\text{H}}$ , and  $g_a$  incremented from 0 to 55 A with  $\delta = 0.8$  ms and  $\Delta = 20$  ms for both resonances. Regression of Eq. (2) onto the normalised echo attenuation plots determined the maximum gradient strength  $g = 17.96 \pm 0.06 \text{ T m}^{-1}$  from the  $^1\text{H}$  plot and  $g = 17.89 \pm 0.02 \text{ T m}^{-1}$  from the  $^2\text{H}$  plot.

**Table 1**  
Maximum gradient strengths determined from a range of current amplitudes

Calibration technique	$g_a$ range (A)	Maximum $g$ ( $T\ m^{-1}$ )
Projection	0–0.6	$17.5 \pm 0.6$
$^1H$ diffusion	0–6	$17.96 \pm 0.06$
$^2H$ diffusion	0–55	$17.89 \pm 0.02$

field strengths. A doubly labelled compound would have the added advantage calibrating against a single diffusion coefficient thus simplifying the method even further. If suitable standards are not available or the probe is incapable of observing other nuclei, observing  $^2H$  nuclei in  $^2H_2O$  can be useful in a two step calibration procedure, e.g. [7], because the initial calibration would be done to a high field strength and consequently artefacts that may arise from eddy currents would be reduced.

In addition to gradient calibration, samples with multiple resonances (especially with high and low  $\gamma$  nuclei) may also be used to assess the presence or absence of eddy currents as a function of  $g$  when  $\tau$ ,  $\delta$ ,  $\Delta$  are kept constant.

Nevertheless, some problems arise when considering lower  $\gamma$  nuclei. First the probe at hand must be capable of observing such nuclei and secondly there is significantly less sensitivity for low  $\gamma$  nuclei which can prevent accurate diffusion measurements.

#### Acknowledgments

This research was supported by a University of Western Sydney Postgraduate Award (N.N.Y.) and a NSW BioFirst Award from the NSW Ministry for Science & Medical Research (W.S.P.). Mr. Gang Zheng is thanked for critically reading the manuscript.

#### References

- [1] W.S. Price, Y. Aihara, K. Hayamizu, NMR studies of nanoscale organization and dynamics in polymer electrolytes, *Aust. J. Chem.* 57 (2004) 1185–1190.
- [2] B.P. Hills, G.A. Webb, Applications of Low-Field NMR to Food Science, Annual Report of NMR Spectroscopy, Academic Press, 2006, pp. 177–230.
- [3] G. Leu, E.J. Fordham, M.D. Hurlimann, P. Frulla, Fixed and pulsed gradient diffusion methods in low-field core analysis, *Magn. Reson. Imaging* 23 (2005) 305–309.
- [4] W.S. Price, Pulsed-field gradient nuclear magnetic resonance as a tool for studying translational diffusion: Part 1, Basic Theory. *Concepts Magn. Reson.* 9 (1997) 299–336.
- [5] P.T. Callaghan, M.E. Komlos, M. Nyden, High magnetic field gradient PGSE NMR in the presence of a large polarizing field, *J. Magn. Reson.* 133 (1998) 177–182.
- [6] P. Galvosas, F. Stallmach, G. Seiffert, J. Kärger, U. Kaess, G. Majer, Generation and application of ultra-high-intensity magnetic field gradient pulses for NMR spectroscopy, *J. Magn. Reson.* 151 (2001) 260–268.
- [7] A.C. Wright, H. Bataille, H.H. Ong, S.L. Wehrli, H.K. Song, F.W. Wehrli, Construction and calibration of a 50 T/M Z-gradient coil for quantitative diffusion microimaging, *J. Magn. Reson.* 186 (2007) 17–25.
- [8] M.I. Hrovat, C.G. Wade, NMR pulsed gradient diffusion measurements. II. Residual gradients and lineshape distortions, *J. Magn. Reson.* 45 (1981) 67–80.
- [9] W.S. Price, K. Hayamizu, H. Ide, Y. Arata, Strategies for diagnosing and alleviating artifactual attenuation associated with large gradient pulses in PGSE NMR diffusion measurements, *J. Magn. Reson.* 139 (1999) 205–212.
- [10] T.W. Nixon, S. McIntyre, D.L. Rothman, R.A. de Graaf, Compensation of gradient-induced magnetic field perturbations, *J. Magn. Reson.* 192 (2008) 209–217.
- [11] W.S. Price, P. Stilbs, B. Jönsson, O. Söderman, Macroscopic background gradient and radiation damping effects on high-field PGSE NMR diffusion measurements, *J. Magn. Reson.* 150 (2001) 49–56.
- [12] N.J. Trappeniers, C.J. Gerritsma, P.H. Oosting, The self-diffusion coefficient of water, at 25 °C, by means of spin-echo technique, *PhL* 18 (1965) 256–257.
- [13] J.S. Murday, Measurement of magnetic field gradient by its effect on the NMR free induction decay, *J. Magn. Reson.* 10 (1973) 111–120.
- [14] D.M. Lamb, P.J. Grandinetti, J. Jonas, Fixed field gradient NMR diffusion measurements using Bessel function fits to the spin-echo signal, *J. Magn. Reson.* 72 (1987) 532–539.
- [15] T.R. Saarinen, C.S. Johnson, Imaging of transient magnetization gratings in NMR. Analogies with laser-induced gratings and applications to diffusion and flow, *J. Magn. Reson.* 78 (1988) 257–270.
- [16] M.I. Hrovat, C.G. Wade, NMR pulsed-gradient diffusion measurements. I. Spin-echo stability and gradient calibration, *J. Magn. Reson.* 44 (1981) 62–75.
- [17] G.H. Sørland, D. Aksnes, Artefacts and pitfalls in diffusion measurements by NMR, *Magn. Reson. Chem.* 40 (2002) S139–S146.
- [18] M. Holz, H. Weingartner, Calibration in accurate spin-echo self-diffusion measurements using  $^1H$  and less-common nuclei, *J. Magn. Reson.* 92 (1991) 115–125.
- [19] M. Holz, S.R. Heil, A. Sacco, Temperature-dependent self-diffusion coefficients of water and six selected molecular liquids for calibration in accurate  $^1H$  NMR PFG measurements, *Phys. Chem. Chem. Phys.* 2 (2000) 4740–4742.
- [20] H. Kato, T. Saito, M. Nabeshima, K. Shimada, S. Kinugasa, Assessment of diffusion coefficients of general solvents by PFG-NMR: investigation of the sources error, *J. Magn. Reson.* 180 (2006) 266–273.
- [21] W.S. Price, H. Ide, Y. Arata, Self-diffusion of supercooled water to 238 K using PGSE NMR diffusion measurements, *J. Phys. Chem. A* 103 (1999) 448–450.
- [22] W.S. Price, H. Ide, Y. Arata, O. Söderman, Temperature dependence of the self-diffusion of supercooled heavy water to 244 K, *J. Phys. Chem. B* 104 (2000) 5874–5876.
- [23] P. Stilbs, Fourier transform pulsed-gradient spin-echo studies of molecular diffusion, *Prog. Nucl. Magn. Reson. Spectrosc.* 19 (1987) 1–45.
- [24] 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.
- [25] R. Mills, Self-diffusion in normal and heavy water in the range 1–45 deg, *J. Phys. Chem.* 77 (1973) 685–688.