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Self-diffusion in nanopores studied by the NMR pulse gradient spin echo

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Abstract – NMR pulse gradient spin echo is the most efficient method for non-invasive elucidation of molecular transport in heterogeneous media. With a proper interpretation of experimental data, the method can also be applied to investigate molecular self-diffusion in pores small enough that the characteristic diffusion times are much shorter than time, needed to build up the spin phase structure by the pulse of magnetic field gradient. This is demonstrated by the analysis of restricted self-diffusion measurement of water molecules trapped in a polyamide membrane. The results are presented as a distribution of spin-relaxation rates and pore sizes in this nanoporous system that also present the method in its true colors as a useful tool in the bio-nanotechology.

Introduction. – Investigation of diffusion phenomena is important in fundamental research, medical and industrial applications, because molecular migration often accompanies or even stipulates the processes in nature. The scientific interest has focused on the development of efficient experimental methods, among which the detection of molecular displacements through the precession of atomic nuclear spins in non-uniform magnetic field by NMR spin echo [1] has gained a decisive role. The method provides insight into transport phenomena on a microscopic level and has achieved a level of sophistication [2,3] that exceeds those being reached by other methods. Stejskal and Tanner [4] initiated the pulsed gradient spin echo method (PGSE) that relies on the use of two sharp pulses of non-uniform magnetic field separated by a well-defined time interval in which the motion of spin-bearing particles affects the spin echo attenuation. They also introduced the methodology of the gradient spin echo as the Fourier transform of the particle probability distribution that leads to the averaged propagator approach (AP) [5–7] providing a way of clear analogy with a tracer spreading in the medium. However, the method needs the gradient pulses to be shorter than the characteristic times of molecular diffusion. For instance, in the case of restricted self-diffusion, the duration of the gradient pulse δ must be much shorter than the time needed for the particle to move across the pore. In addition, strong gradient pulses G are required. Namely, a pulse creates spatial spin dephasing, $q = \gamma G\delta$, or phase grating, that can be described by its wavelength. This wavelength has to be shorter than the compartment size, but the self-induction of gradient coils puts the limit to fast switching time of magnetic field gradient, and these conditions cannot always be fulfilled. For instance, the analysis of PGSE measurements of water restricted diffusion by the AP method is limited to pores larger than a few μm. In smaller pores, the effect of molecular motion during the buildup of a spin phase structure by applied gradient pulse has to be taken into account.

By taking into account the stochastic nature of molecular self-diffusion we can expand the gradient spin echo in the cumulant series with respect to the parameter of spin dephasing, q [8]. The expansion to the second order [9,10] leads to the Gaussian phase approximation (GPA), which enables the analysis of PGSE measurements with finite duration of gradient pulses. However, the method is commonly considered as an insufficient approximation for the analysis of PGSE measurements of restricted diffusion [11] particularly due to its inability to describe

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the diffusive diffraction of spin echo [12]. Therefore, different more sophisticated techniques have been invented to analyze the data obtained by the finite width PGSE [6,13,14]. The allegation of GPA inadequacy results from commonly accepted but false use of the "Gaussian approximation", with ensemble-averaged terms of cumulant expansion. The ensemble average cancels the first cumulant term that is responsible for the undulation of spin echo featuring as a "diffusive diffraction" [15]. Taking the ensemble average at the very beginning contradicts the approach proposed by Hahn [1] and Carr and Purcell [2] a long ago. They suggested that the spin dynamics of each individual molecule in its translational Brownian motion has to be followed throughout the experiment but the total, ensemble-averaged magnetic moment of spins is evaluated at the very end, *i.e.*, at the time of signal acquisition. If calculated this way, the gradient spin echo attenuation in GPA shows an almost identical diffraction-like feature [16] as that obtained by the exact AP method [17–20]. Therefore, we distinguish the "correct" GPA from that with the ensemble-averaged cumulants by naming the last one as a "normal distribution approximation" (NDA). For the case of restricted diffusion measurement by short PGSE sequence, ref. [15] shows that the q-space Fourier transform of spin echo attenuation calculated by the exact AP, GPA and NDA method results in almost identical bell-shaped propagators with identical second moments, but with small differences in the kurtosis in the case of simple geometry. This means that the first cumulant term of GPA, which describes the "diffusive diffractions" of spin echo, contributes only a small modification to the shape of diffusion propagator and thus contains a minor correction to information about the porous structure delivered by PGSE method.

In the case of short gradient pulses, the cumulant series converges into the GPA for sufficiently small values of $q\,\partial v\,\tau_c \approx q\,a < 1$, in which ∂v is the velocity fluctuation, and τ_c is the characteristic time of particle diffusion across the pore of diameter a [21]. In the following we show that the sequence with gradient pulses such that $\delta > \tau_c$ weakens the above restriction to $q\,a\frac{\tau_c}{\delta} < 1$, which indicates even a faster convergence of cumulant series.

All the above leads to the conclusion that either GPA or even its simpler variant NDA are appropriate methods for the analysis of data obtained by the PGSE with finite width gradient pulses, if the experimental data are treated as shown in the following.

PGSE with finite gradient pulses and self-diffusion in nanopores. – Neglecting spin relaxation and by following the procedure described in refs. [15,16], the pulse gradient spin echo in GPA

$$E(\Delta,\delta,q) = \sum_j \mathrm{e}^{iq\langle\xi(\Delta,\delta)\rangle_j - \frac{q^2}{2}\langle\xi^2(\Delta,\delta)\rangle_j + \cdots}, \qquad (1)$$

in which the sum over j represents a sum over individual spins and ξ is apparent fluctuation of spin position along the direction of magnetic gradient z. The q-space Fourier transform of eq. (1) gives the propagator in the form of the sum of normal distributions shifted from the origin by the first cumulant terms, $\langle\xi(\Delta,\delta)\rangle_j$, which are also responsible for the diffraction patterns as shown in ref. [16]. In the case of short PGSE, the shape of this multi-normal distribution does not differ significantly from that obtained using the exact calculation with AP [15] or by using NDA. Thus, we presume that NDA is sufficient for the analysis of data obtained by the finite width PGSE sequence, if data are treated with the q-space Fourier transform:

$$\begin{aligned} FT\left[E(q)\right](z) &\approx FT\left[\mathrm{e}^{-\frac{q^2}{2}M_2}\right](z) \\ &= \frac{1}{\sqrt{M_2}}\,\mathrm{e}^{-\frac{z^2}{2M_2}}. \end{aligned} \qquad (2)$$

Here, the cumulant terms of GPA in eq. (1) are substituted by the ensemble averages values, $\overline{\langle\xi(\Delta,\delta)\rangle} = \frac{1}{N}\sum_j \langle\xi(\Delta,\delta)\rangle_j = 0$ and $M_2 = \overline{\langle\xi^2(\Delta,\delta)\rangle} = \frac{1}{N}\sum_j \langle\xi^2(\Delta,\delta)\rangle_j$, which is the second moment of the propagator. The probability distribution spreading of confined spins can be calculated from the Fick's diffusion equation

$$P(\mathbf{r},t|\mathbf{r}_j) = \sum_k \psi_k(\mathbf{r})\psi_k(\mathbf{r}_j)\,\mathrm{e}^{-\frac{t}{\tau_k}}, \qquad (3)$$

in which the pore boundary conditions define the set of eigen functions and characteristic times, $\{\psi_{\mathbf{k}},\tau_k\}$. The second moment of the resulting propagator is

$$M_2 = \overline{\langle\xi^2(\Delta,\delta)\rangle} = \sum_k b_k g(\Delta,\delta,\tau_k), \qquad (4)$$

in which $b_k = \int\int (z-z')^2\psi_k(\mathbf{r})\psi_k(\mathbf{r}')\mathrm{d}\mathbf{r}'\mathrm{d}\mathbf{r}$. With $q(t) = \gamma\int G_{eff}(t)\mathrm{d}t$, in which $G_{eff}(t)$ is the effective gradient of PGSE sequence [10], the effect of the gradient pulse timing and the diffusion correlation times can be evaluated as

$$\begin{aligned} g(\Delta,\delta,\tau_k) &= \frac{2}{q^2}\int_0^{\Delta+\delta}\int_0^t q(t)q(t')\,\mathrm{e}^{-\frac{t-t'}{\tau_k}}\,\mathrm{d}t'\mathrm{d}t \\ &= \frac{2\tau_k^2}{\delta^2}\left(2\left(\frac{\delta}{\tau_k} - 1 + \mathrm{e}^{-\frac{\delta}{\tau_k}}\right)\right. \\ &\quad \left. - \mathrm{e}^{-\frac{\Delta+\delta}{\tau_k}}\left(1-\mathrm{e}^{\frac{\delta}{\tau_k}}\right)^2\right). \end{aligned} \qquad (5)$$

With this result any PGSE diffusion measurement can be analyzed very generally. In the case of diffusion in a pore large enough that the short gradient pulse approximation is valid, $\delta \ll \Delta,\tau_k$ (or a regime of "slow diffusion" [22]), the second moment is

$$M_{2l} = \sum_k b_k(1 - \mathrm{e}^{-\Delta/\tau_k} - \frac{\delta}{3\tau_k} + \ldots). \qquad (6)$$

In the other extreme of diffusion in a very small pore, when $\tau_k \ll \delta$ (or "a motional narrowing regime" [22]), the above equations give the second moment

$$M_{2s} = 4\sum_k b_k\frac{\tau_k}{\delta} + \ldots \approx k_1\frac{r^4}{D\delta}. \qquad (7)$$

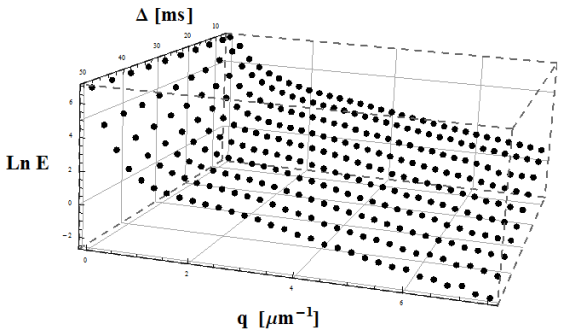

Fig. 1: Spin echo dependence on $q = \gamma G\delta$ for different Δ at PGSE measurement of porous polyamid membrane.

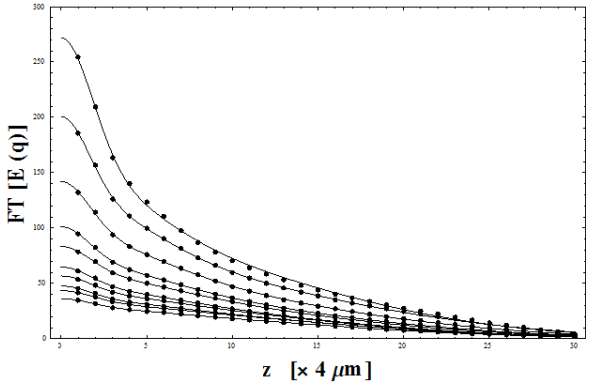

Fig. 2: q-space Fourier transform of experimental data (points) fitted by multi-normal distributions (curves).

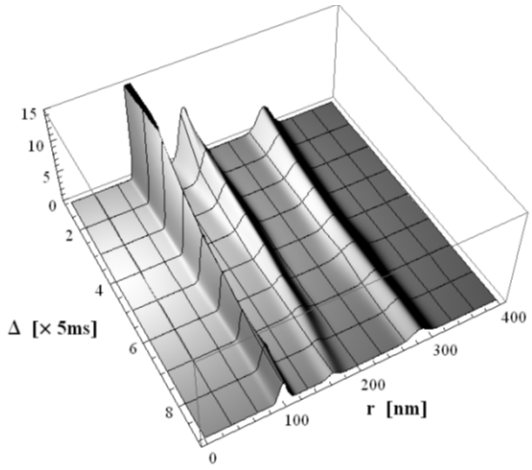

Fig. 3: Amplitudes of propagators as a function of Δ and the radius of pores calculated from the second moments M_{2s} using eq. (7) for the case of spherical pore.

The second moment, which is proportional to the fourth power of the pore radius r reduced by the ratio between the particle transversal time across the pore and the duration of the gradient pulse, has been derived also in other ways [12,23]. Factor k_1 depends on the pore geometry and the alignment in the magnetic field gradient. For spherical pores $k_1 = 0.256$, while for randomly distributed cylindrical pores $k_1 = 0.390$.

In a very heterogeneous porous material, a broad dispersion of pore sizes is expected with ranges from a few nanometer to a few micrometers. The magnetization sink at the boundaries causes differences in spin relaxation in pores of different sizes, *i.e.* the relaxation time is shorter in smaller pores. Thus, the diffusion propagator of such a sample consists of many normal distributions that decay differently with the spin-relaxation times T_{1p} as

$$FT\left[E(q)\right](z) \approx \sum_p N_p \frac{1}{\sqrt{2\pi M_{2p}}} \mathrm{e}^{-\frac{z^2}{2M_{2p}} - \frac{\Delta+\delta}{T_{1p}}}, \qquad (8)$$

where N_p is the number of spins in pores of different size in the sample.

Experiment and discussion. – Experiments have been performed on a Bruker AVANCE 500 NMR spectrometer operating on the proton resonance frequency 500 MHz and equipped with a diffusion probe Diff30 generating a maximum amplitude of the pulsed field gradient of $G = 12\,\mathrm{T/m}$ to test the above theory by measuring restricted self-diffusion in a porous Poly(amide)-6 (PA-6) membrane [24]. Polyamid membrane, which is developed for the mechanical filters of solutions, is very hydrophilic and mechanically strong, and as such adequate for the characterization by PGSE method. The membrane sample was tightly rolled and soaked with distilled water. The scroll axis was perpendicular to the magnetic field gradient. In the previous study of this material, the method of stimulated gradient spin echo [25] with the diffusion time ranging from 100 to 900 ms was used to obtain information about 4 μm pores consisting the structure of the sample, which nicely compares to structures found in electron micrographs. The aim of our complementary experiment was to get information about the self-diffusion in smaller pores by inspecting the range of shorter diffusion times. The measurements were performed by using a PGSE sequence with fixed pulse width $\delta = 2.5$ ms, but at the variable interval between gradient pulses Δ from 7 ms to 50 ms and by changing the magnetic field gradient in 64 identical steps from zero to 11.60 T/m at temperature of 22 °C.

Experimental results in fig. 1 show the spin echo dependence on q that exhibits a decay with small undulations, which are particularly clear at long Δ. They display the diffraction features described by the first cumulat term of GPA, and demonstrate the uselessness of the inverse-Laplace transform method [26] for the extraction of pore distribution in this case. However, three different normal functions were sufficient for an adequate fit of the diffusion propagators obtained by the q-space cosine Fourier transform of experimental data as shown in fig. 2. Second moments of extracted propagators remain fixed as the interval between gradient pulses, Δ, changes. This is a

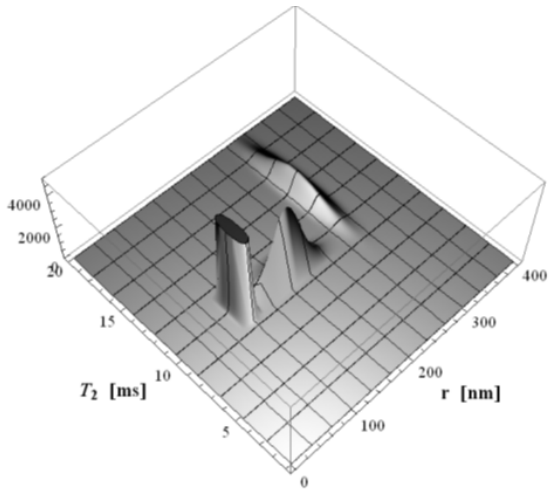

Fig. 4: Size and spin-relaxation distribution of pores in polyamid membrane.

clear indication of the regime of long gradient pulses with $\tau_k < \delta$, in which molecular motion affects spin echo attenuation mostly during the creation of spin phase structure. Previous derivation leading to eq. (7) shows that the size of pores can be obtained from the fourth root of the second moments with given k_1, water self-diffusion D, and gradient pulse width δ. By assuming spherical pores, fig. 3 shows the amplitudes of propagators, whose second moments, and corresponding pore radii, do not depend on the interval between pulses, Δ, but the decays of amplitudes give the spin relaxation of water in different pores. A combined 3-D plot in fig. 4 shows the spin-relaxation distribution and the pore radius distribution broadened by the uncertainties of the fitting parameters. The plot shows the prevailing share of spins in the pores with the radius $r = (100 \pm 10)$ nm (70%) and in the pores with the radius (175 ± 30) nm (20%). Water in these two types of pores has almost identical spin relaxation $T_2 = (10 \pm 2)$ ms, while water in the pores with the radius of $r = (282 \pm 7)$ nm (5%) have a broader distribution of relaxation times, $T_2 = (14 \pm 5)$ ms.

The experiment provides information on the nanopore structure in the polyamide membrane, that was not seen in the previous investigation by the method of stimulated gradient spin echo [25]. Its results also confirm GPA suitability for the analysis of spin echo diffusion measurements, when the finite width of magnetic gradient pulses cannot be neglected and lead to the conclusion that the NMR PGSE method has a potential to become a standard method for the characterization of nanoporous systems, and as such also a useful tool in bio-nanotechology.

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