Molecular velocity auto-correlations in glycerol/water mixtures studied by NMR MGSE method[☆]

Janez Stepišnik [a],[*], Carlos Mattea [c], Siegfried Stapf [c], Aleš Mohorič [a],[b]

[a] University of Ljubljana, Faculty of Mathematics and Physics, Physics Department, Jadranska 19, 1000 Ljubljana, Slovenia
[b] Dept. Technical Physics II, TU Ilmenau, 98684 Ilmenau, Germany
[c] Institute Jožef Stefan, Jamova 39, 1000 Ljubljana, Slovenia

ABSTRACT

Molecular dynamics in binary mixtures of water and glycerol was studied by measuring the spectrum of water velocity auto-correlation in the frequency range from $0.05 - 10$ kHz by using the NMR method of modulated gradient spin echo. The method shows that the diversity of diffusion signature in the short spin trajectories provides information about heterogeneity of molecular motion due to the motion in the micro-vortexes of hydrodynamic fluctuation, which is especially pronounced for the mixtures with low glycerol content. As concentration of glycerol increases above 10vol%, a new feature of spectrum appears due to interaction of water molecules with the clusters formed around hydrophilic glycerol molecules. New spectrum exposes a rate thickening of molecular friction, according to Einstein–Smoluchowski–Kubo formula, which inhibits rapid molecular motions and creates the conditions for a slow process of spontaneously folding of disordered poly-peptides into biologically active protein molecules when immersed in such a mixture.

1. Introduction

Earliest models of liquids as totally disordered structures have been replaced by models of systems with a long range-disordered and short range-ordered systems where molecules can associate in clusters [1,2] due to intermolecular interactions [3,4], but there is still lack of understanding of molecular dynamic that plays an important role in biological systems. It refers primarily to liquids with hydrogen bonding such as water, alcohol, glycerol and mixtures thereof. The molecular mechanisms of these liquids, which spontaneously folds a disordered poly-peptide into the unique structure of a biologically active protein molecule, when immersed in them, are still not understood. Particularly pronounced in maintaining the structure of biologically active macromolecules and promoting protein self-assembly are glycerol–water (G/W) mixtures [5]. Despite considerable research efforts [6,7] these questions remain among the key unresolved issues in soft condensed matter physics, physical chemistry, materials science and biophysics.

The G/W mixtures have already been a subject of extensive research involving thermodynamic measurements [8], broadband dielectric measurement [9,10], NMR [11–13], infrared (IR) [5], and Raman spectroscopy [14], etc. These

studies reveal changes in the aqueous structure beyond the first neighbor level, but general properties of the G/W mixtures and how they affect the molecular dynamics are not revealed. They also show that macrophages are formed, because the glycerol is a small molecule of trihydric alcohol with large affinity to form 3D hydrogen-bonded network pervading the bulk of mixtures [15–17]. Hydrogen bond energy between glycerol molecules (0.25 eV) and between water (0.19 eV) are lower than the binding energy between water and glycerol molecules (0.29 eV), leading to the molecular clusterization [18] confirmed by the dielectric measurements with almost tri-fold increase of the activation enthalpy of 0.9 mol% G/W mixture compared to the pure water at $H = 16.2$ kJ/mol [19].

In liquids the thermal molecular motion is impeded by interactions with its neighbors. Velocity auto-correlation function (VAF) is a quantity containing information about the underlying processes of molecular interaction and dynamics [20]. The VAF, which is associated with a number of physical properties, such as thermal and mass diffusion, sound propagation, transverse-wave excitation, and can have either a single-particle or a collective nature, has a profound meaning in the statistical physics of fluids [6,7,21], but it is extremely difficult to measure. Some information can be obtained by neutron scattering [22–24] and light scattering [25], but a short time scale of these methods cannot extracts information of its long time properties. This leads to the conclusion that the computer simulation of molecular dynamics is the most suitable tool for the study of translation dynamics in molecular systems [26,15]. The current understanding of molecular dynamics in G/W mixtures is derived from experimental results in combination with computer simulations. Simulations can reproduce some macroscopic physical properties, but they largely depend on the chosen models. Thus, conclusions derived from models regarding molecular structure and dynamics remain uncertain [27].

A lot of effort has been devoted toward understanding of the molecular translation dynamics in water, glycerol and G/W mixtures by measuring the self-diffusion coefficient, D. Well known are the studies of molecular dynamics in liquids by measuring D in water by tracer technique [28], the measurements in the G/W mixtures by using the interferometric micro-diffusion method [29] and by NMR methods [30,13]. The results of tracer technique are commonly used to calibrate the diffusion measurements done by other techniques, especially those obtained by the NMR gradient spin echo method [31,32]. This method uses the magnetic field gradient $\nabla|\mathbf{B}| = \mathbf{G}$ (MFG) to detect the translation displacement of molecules via uneven precession of their atomic nuclear spins. A variant of this method, the pulsed gradient spin-echo (PGSE), provides the signal attenuation proportional to the molecular mean squared displacement (MSD) in the interval between two consecutive MFG pulses [33,34]. However, the PGSE measurements in water at different pressures and temperatures [35,36] show values of D scattered beyond the experimental uncertainty [28]. Differences are commonly assigned to inaccurately calibrated MFG or to the convection flows in liquids. However, differences may also be due to the failure to observe properly some of experimental parameters as shown in the following. In the measurement of G/W mixture by the stimulated PGSE technique [37], only D of water is obtained, since its contribution to the NMR signal is well distinguished by glycerol. The study proves the validity of the Arrhenius behavior and the Stokes–Einstein relationship between D and viscosity η in the range of around room temperatures, but with deviations at temperatures close to the glass transition. The diffusion in G/W mixtures was measured also with the PGSE-FT NMR method by measuring the NMR hydrogen signal of CH_2, and OH to which both water and glycerol contribute [13]. Since the proton exchange between hydroxy groups of glycerol and water is much faster than the time intervals of spin-echo sequence, D of water component was calculated by taking into account numbers of OH groups belonging to water and glycerol molecules. The mutual diffusion coefficient of G/W mixtures was also measured by the Gouy interferometric technique, but these results return substantially higher D than obtained by the interferometric micro-diffusion method [29] and lower than measured by the holographic interferometry [38]. No evident reason for these discrepancies has been found [13].

According to the Einstein definition [39], D is a time derivative of the molecular mean squared displacement (MSD) in the long time limit. When measured in a finite time interval, as in the case of the PGSE methods, D can exhibit time dependence, because the initial velocity of labeled molecule, $\mathbf{v}(t)$, may not be forgotten fast enough. Thus, D obtained by this method may be different from that obtained by tracer techniques. According to the Green–Kubo formula [20] the measurement in the finite time interval gives

$$D_{zz}(\tau) = \int_0^\tau \langle v_z(t)v_z(0)\rangle_\tau dt = \frac{2}{\pi}\int_0^\infty D_{zz}(\omega)_\tau \frac{\sin(\tau\omega)}{\omega}d\omega, \tag{1}$$

which is the time-dependent self-diffusion coefficient, $D_{zz}(\tau)$ for the motion along z-direction in the diffusion interval τ. It is related to the power spectrum i.e. the velocity autocorrelation spectrum (VAS)

$$D_{zz}(\omega)_\tau = \int_0^\tau \langle v_z(t)v_z(0)\rangle_\tau \cos(\omega t)dt,$$

where $\langle ...\rangle_\tau$ indicates the ensemble average over the particle trajectories in the interval τ.

Theories [40–43] and simulations [44–46] predict a long-time asymptote of the VAF as the $t^{-3/2}$-long time tail in liquids. Recent studies by the NMR modulated gradient spin-echo (MGSE) method [47] have shown a deviation from this asymptotic properties in simple liquids such as water, ethanol and glycerol due to inter-molecular interactions. In these measurements the unusual heterogeneity of molecular motion is observed, when the measurement interval is very short, which one cannot describe by a simple diffusion coefficient. In order to enlighten these phenomena and the function of glycerol as a colligative solute we set out to study the molecular self-diffusion in G/W mixtures by the NMR MGSE method presented in the following.

2. NMR gradient spin-echo method

In liquids rapid molecular motion on the time scale of pico- or nanoseconds completely nullifies the spin dipole–dipole and the first order quadrupole interactions, while the spin interactions with electrons in molecular orbitals and the electron mediated spin–spin interactions cannot be ignored. They appear as the chemical shifts and *J*-couplings in the NMR spectrum. Fluctuation of these interactions can be characterized by correlation functions of relevant physical quantities and affect spin relaxation. In the gradient spin echo method, the applied MFG is commonly strong enough that the effect of fluctuation of molecular translation velocity prevails in echo attenuation over all other interactions. NMR gradient spin echo sequences create the spatial spin phase discord described by its wave vector, $\mathbf{q}(t) = \gamma \int_0^t \mathbf{G}(t') f_\pi(t') dt'$, in which π-RF pulses switch $b(t')$ in $f_\pi(t) = \int_0^t \cos(b(t')) dt'$ between $\pm \pi$ [48]. Whenever the molecular displacements within the interval of phase modulation are shorter than $1/|\mathbf{q}|$, the decay of signal of the spin-echo peak at the time τ can be approximated by the cumulant series in the Gaussian approximation as [49–51]

$$E(\tau) = \sum_i E_{oi} \, e^{-i\alpha_i(\tau) - \beta_i(\tau)}. \tag{2}$$

Here the sum goes over the sub-ensembles of spins with identical dynamical properties. The phase shift

$$\alpha_i(\tau) = \int_0^\tau \mathbf{q}(t) \cdot \langle \mathbf{v}_i(t) \rangle dt, \tag{3}$$

can be neglected, when the averaged velocity of spin bearing particle is zero, $\langle \mathbf{v}_i(t) \rangle = 0$. This it is not in the case of collective molecular motion or diffusion in non-homogeneous systems like porous media [51].

Spin-echo attenuation is given by [50]

$$\beta_i(\tau) = \frac{1}{\pi} \int_0^\infty \mathbf{q}(\omega, \tau) \mathbf{D}_i(\omega, \tau) \mathbf{q}^*(\omega, \tau) \, d\omega, \tag{4}$$

where $\mathbf{q}(\omega, \tau)$ is the spectrum of the spin phase discord $\mathbf{q}(t)$ [47] and where the VAS is

$$\mathbf{D}_i(\omega, \tau) = \int_0^\infty \langle \mathbf{v}_i(t) \otimes \mathbf{v}_i(0) \rangle_\tau \cos(\omega t) dt. \tag{5}$$

According to Eq. (4), the measurement of liquid by the pulsed gradient spin echo (PGSE) sequence, which consists of two MFG pulses of width δ and separated for Δ, gives the spin echo attenuation in liquids [52]

$$\beta_i(\Delta, \delta) = \frac{\gamma^2 G^2}{\pi} \int_0^\infty D(\omega) \left(\frac{4 \sin(\omega \delta/2) \sin(\omega \Delta/2)}{\omega^2} \right)^2 d\omega, \tag{6}$$

from which $D(\omega)$ and thus $D(t)$ can be extracted with considerable difficulty by changing Δ and δ if they are in the range of VAF correlation time τ_c. At the present state of the art, the MFG coil induction limits the width and the shape of the MFG pulses to above 1 ms, which is close to or slightly above values of τ_c in some liquids [47]. Thus, neglecting the dependence of the echo decay on δ and Δ according to Eq. (6), when measuring the self-diffusion in water by PGSE method, gives an apparent self-diffusion coefficients that may differ from one another [28,35,36] and also deviate from those obtained from the theory and the simulations of molecular dynamics and water binary mixtures [53,54].

The determination of the long time asymptotic properties of VAF in dense systems is still a challenge that can be tackled by a NMR method, which directly probes the VAS. Such method is the modulated gradient spin echo [50], where the sequence of RF-pulses and MFG modulates the spatial dispersion of the spin phase. The method is basically a Carr–Purcell–Meiboom–Gill sequence (CPMG) consisting of initial $\pi/2$-RF-pulse and the train of N π-RF pulses separated by time intervals T [32,55], which was used initially to reduce the effect of diffusion in the measurement of T_2 relaxation. Detailed analysis shows that the sequence imprints information about VAS, when applied in the combination with MFG [49,56]. In first applications of MGSE method, pulsed or oscillating MFG were used to measure water flow through porous material [57] and molecular restricted self-diffusion in porous media [58–61]. It was also demonstrated how the MGSE sequence improves the resolution of the diffusion-weighted MR images of the brain and the MRI of the diffusion tensor of neurons [62]. As in the case of PGSE, the frequency range of MGSE with the pulsed MFG is limited to below 1 kHz due to the gradient coil self-inductance. With the development of the MGSE technique in constant MFG, the frequency induction limit was avoided. New technique enables higher frequency limit, which is now determined by the power of the RF transmitter and the magnitude of the MFG, while the lowest limit is inversely proportional the spin relaxation time. The use of the MGSE techniques with fixed MFG was first proposed in Ref. [50] with concern about the side effects of using RF pulses in the presence of background MFG. Analysis of adverse interferences of both fields [48,47] shows that at suitable experimental conditions the MGSE signal decay can be described as

$$E(\tau, \omega_m) = \sum_i E_{oi} \, e^{-\frac{\tau}{T_{2i}} - \frac{8\gamma^2 G^2}{\pi^2 \omega_m^2} D_{zzi}(\omega_m, \tau)\tau}. \tag{7}$$
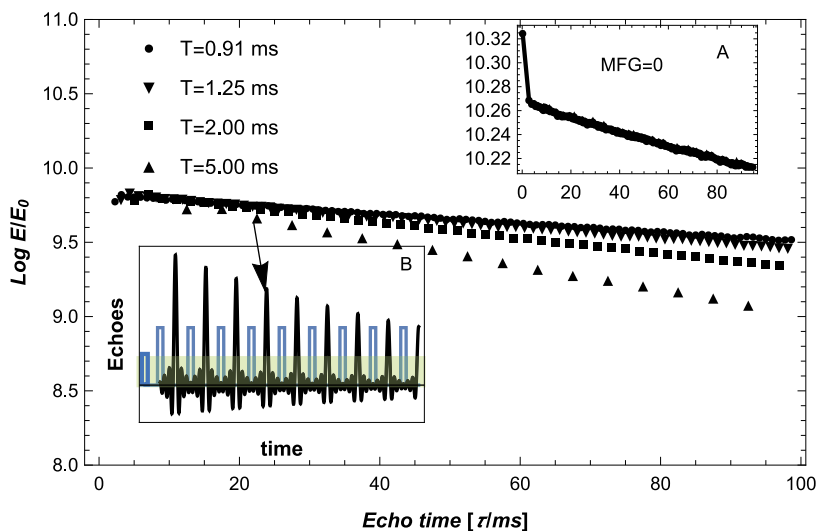
Fig. 1. MGSE spin echo decays in a mixture of 20 vol% glycerol in water at different modulation frequencies ($\omega = \pi/T$). The inserted images show: (A) the signal decay in zero MFG and (B) MGSE sequence with RF pulses (blue) and MFG (green) giving spin echoes (black) whose peaks contain information about molecular motion.

Here, $\tau = NT$ and $D_{zzi}(\omega_m, \tau)$ denotes the component of VAS tensor of the ith spin sub-ensemble in the direction of applied MFG at the modulation frequency $\omega_m = \pi/T$ averaged over the interval τ, and where T_{2i} is the spin relaxation time. The advantage of the new MGSE technique was demonstrated by measuring the VAS of restricted diffusion in pores smaller than 0.1 μm [48], by measuring the VAS of granular dynamics in fluidized granular systems [63] and by the discovery of a new low frequency mode of motion in polymer melts [64]. Instead of using the externally applied MFG, this MGSE method also allows the exploitation of MFG generated by the susceptibility differences on interfaces in porous systems to obtain information about the pore morphology and distribution of internal MFG [48].

3. Experiments

NMR spectrometer with 100 MHz proton Larmor frequency equipped with the Maxwell gradient coils to generate MFG in steps to the maximum of 5.7 T/m was used to measure the VAS of in G/W mixtures at room temperatures by the MGSE method. Only water echoes are traced, as the contribution of glycerol to signal decay can be neglected due to its slow diffusion rate and short spin relaxation time. Results were checked by repeated measurements of the same samples on the NMR-MOUSE [65] operating at 18, 7 MHz proton Larmor frequency with fixed MFG of 21.6 T/m. The high magnetic field of the 100 MHz spectrometer allows measurements with a high signal to noise ratio, but with the top frequency limited to 3 kHz due to the weak MFG. On the other hand, the large MFG of one-sided magnet of the NMR MOUSE allows measurements of very slow diffusion in the frequency range up to about 10 kHz. However, its fix MFG limits the measurements on G/W mixtures to below 1 kHz due to fast diffusion rate of water.

Samples of pure glycerol (99.5%-Sigma-Aldrich), distillate water and mixtures with several different volume fractions of glycerol were prepared in plastic bottles of 100 ml volume. Tightly sealed with a plastic lid were kept for several days before used for the measurements. The samples were loaded into 15 mm long and 5 mm wide pyrex glass ampules and closed with paraffin tape to be inserted in the head of the 100 MHz NMR spectrometer. While the flat shelf of one-sided magnet of the NMR-MOUSE allows the measurements of mixtures in bottles without the loading step. In order to avoid a possible impact of restricted diffusion, containers with the diameter much larger than the molecular displacements in the time of 100 ms long intervals of measurement were used. In addition, the effect of restricted diffusion is even further reduced by the initial $\pi/2$-RF pulse of the MGSE sequence applied in the background of MFG, because it excites only a few mm narrow slice of sample.

In the measurements on the 100 MHz NMR device, the amplitudes of echo peaks are recorded in the time interval of 100 ms. Measurements are repeated with different T and magnitude of MFG, G, in a way to keep the product $T \times G = const$. Fig. 1 shows that the number of recorded peaks increases with the shortening of T. In this way the exponential decay of N-echo peaks is effected only by the changes of $D(\omega, \tau)$ at the frequency $\omega = \pi/T$, where τ denotes average over the interval $\tau = NT$. The contribution of spin relaxation to the signal decay is determined by separate measurements in zero MFG as shown in the inset picture in Fig. 1. The spin relaxation exhibits almost a clear mono-exponential decay, except in the initial interval of a few milliseconds, with the rapid decay believed to belong to water bounded in clusters.
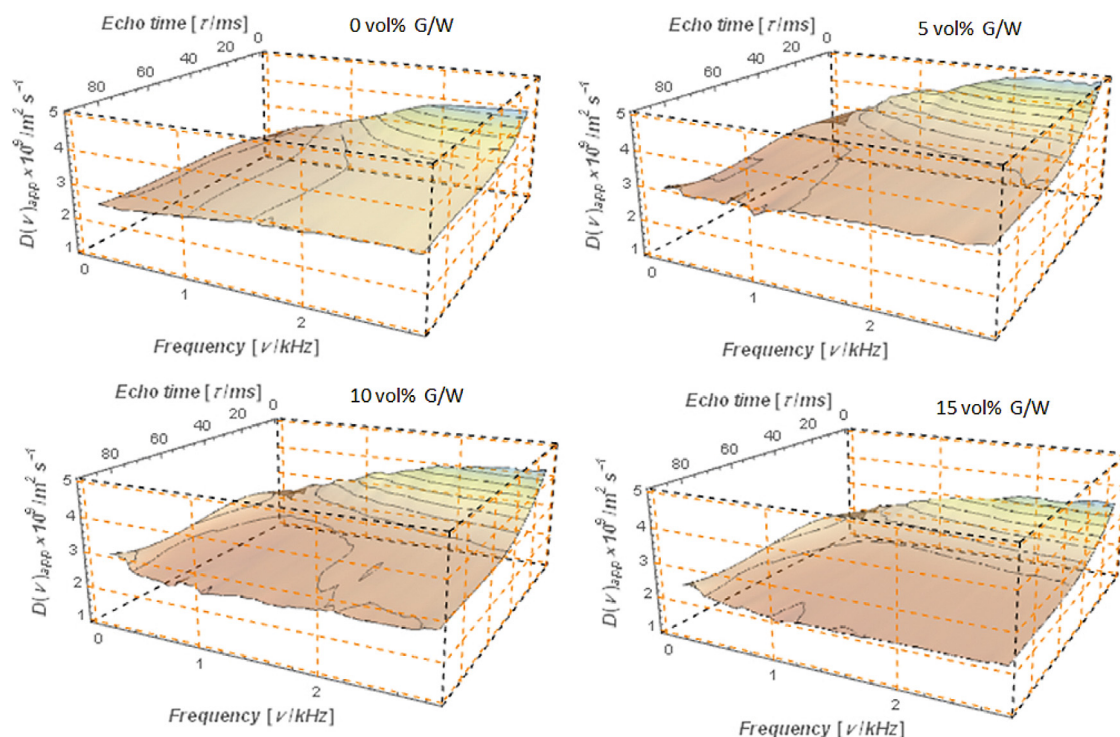
Fig. 2. 3D temporal-frequency plots of apparent VAS for the G/W mixtures with 0 vol%, 5 vol%, 10 vol%, 15 vol% of glycerol.
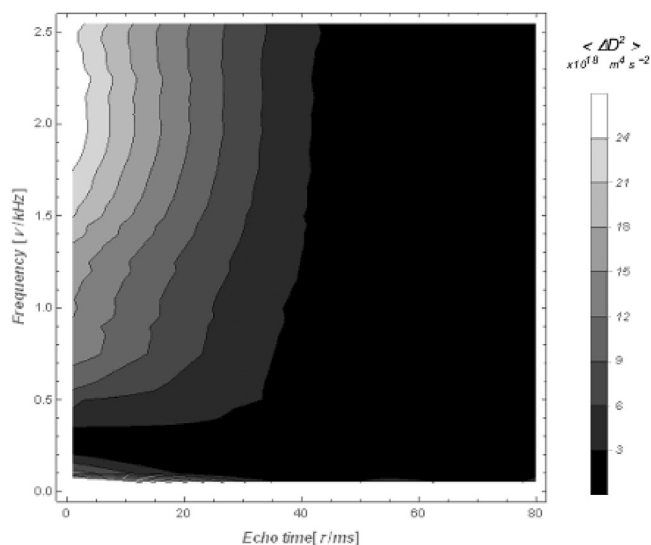

Fig. 3. The contour plot of the distribution variance of the diffusion coefficient, $\langle \Delta D^2 \rangle$, for the G/W mixture with 5 vol% of glycerol showing the diversity of molecular motion observed only at short observation times and at high modulation frequencies.

4. Results and discussion

Data was analyzed in the following way. A fifth order polynomial is fitted to the series of echo peak amplitudes with given T as a function of time τ. The time derivative of this fit represents the diffusion spectrum if the spin relaxation is accounted for by proper normalization of the echo decay. The MGSE measurements of G/W mixtures on the 100 MHz NMR device give time dependencies of spin-echoes $E(\tau)$ that deviate from the anticipated mono-exponential decays particularly in pure water and G/W mixtures with lower glycerol contents. The deviations are clearly visible in the 3D
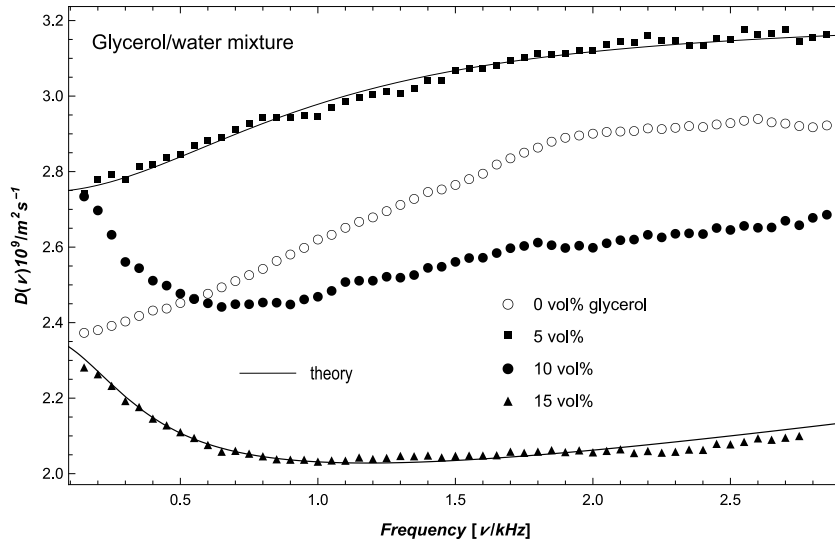
Fig. 4. The dots show VAS of G/W mixtures measured at echo times $\tau > 50$ ms and the fitting curves correspond to the harmonic couplings of diffusing particles described with Eq. (11) for 5 vol% and with Eq. (12) for 15 vol% of glycerol content.

frequency/temporal plots $D(\omega, \tau)$ of the time derivatives of curves obtained by fitting the echo peaks with the coefficient of determination of $R^2 > 0.99999$ shown in Figs. 2 and 6. Instead of constant value along the echo time, τ, anticipated for the mono-exponential decays, discrepancies occur that cause the 3D plots to show a curved surface at short intervals τ and of higher frequencies. In the case of simple liquids [47], we interpreted similar curved surface by the molecular diffusion diversity due to the motion in the vortexes of hydrodynamic fluctuations. Namely, during initial interval after the spin excitation, when the trajectories of the molecules are still short, the spins may observe local inhomogeneity caused by the distribution of internal MFG in the porous medium [47] or motional diversity due to fluxes or hydrodynamic oscillation in liquids [48]. By grouping the spin bearing particles into separate sub-ensembles corresponding to spins with the different spin-echo attenuation, we can describe the induction signal with the distribution function $P(D)$ as $E(\tau) = \int P(D)e^{-sD\tau} dD$ with $s = \frac{8\gamma^2 G^2}{\pi^2 \omega^2}$ given in Eq. (7). In the case of narrow distribution, the signal attenuation can be approximated by

$$\log E = \beta(\tau) \approx -\tau/T_2 - s\langle D\rangle\tau + \frac{s^2}{2}\langle\Delta D^2\rangle\tau^2 + \cdots \tag{8}$$

Here $\langle D\rangle$ is the mean diffusion coefficient and $\langle\Delta D^2\rangle$ is the variance of distribution. In the cases of a non-exponential decay the time derivative of echo attenuation does not give VAS, but some apparent one, $D_{app}(\omega, \tau)$, which conveys information on the mean diffusion coefficient and its distribution. 3D frequency/temporal plots of $D_{app}(\omega, \tau)$ for pure water and for G/W mixtures with 0.05, 0.10 and 0.15 volume fraction of glycerol are shown in Fig. 2 and for the G/W mixtures with 0.20, 0.33, 0.50 and 0.66 volume fraction of glycerol in Fig. 5. In water and mixtures with the lower glycerol content a curved surface is evident in the 3D plots of spectra in the range of short τ and at higher frequencies due to the distribution of the self-diffusion coefficients. The part of curved surface is clearly visible in the contour plot of the second derivative of $\beta(\tau)$ of the mixture with 5 vol% of glycerol content in Fig. 3, which shows how $\langle\Delta D^2\rangle$ occurs at high modulation frequencies and disappears with increasing echo-time at $\tau > 40$ ms, when the trajectories of spins become long enough to span the whole extend of heterogeneity and to average off the diffusion diversity into $\langle\Delta D^2\rangle = 0$, what is also seen in Figs. 2 and 6. Similar diversity was observed in the MGSE measurements of VAS in water, ethanol and toluene with the explanation of the molecular self-diffusion in the vortexes of hydrodynamic fluctuations [47].

By increasing the glycerol content, the curved surface of spectra is reduced, but in the mixtures with ≥ 10 vol% of glycerol a new spectral feature appears in the form of a low frequency ridge that levels at higher frequencies. In order to enhance visibility of spectral changes and to avoid the part affected by hydrodynamic fluctuation, where $\langle\Delta D^2\rangle \neq 0$, we present in Fig. 4 the VAS at echo times $\tau > 50$ ms for the mixtures with 0.00, 0.05, 0.10 and 0.15 vol% of glycerol. The spectrum of mixture with 5 vol% of glycerol has a form similar to that of pure water, only shifted up-wards by about 30%. The upwards shift indicates a disruption of hydrogen bonding in water caused by a low glycerol content in water. A drastic change of spectra appears at the concentrations of 10 and 15 vol% of glycerol indicating new type of inter-molecular interaction, which has a strong impact on the molecular dynamics. 3D presentations of spectra in Figs. 2 and 5 clearly show how the increase of glycerol content lowers the spectrum level, reduces the spectral hump, i.e. the curved surface at short τ, which is attributed to the bulk water. The low frequency ridge of the new spectrum, which starts to appear at 10 vol% of glycerol, remains almost unchanged with the increase of glycerol content.
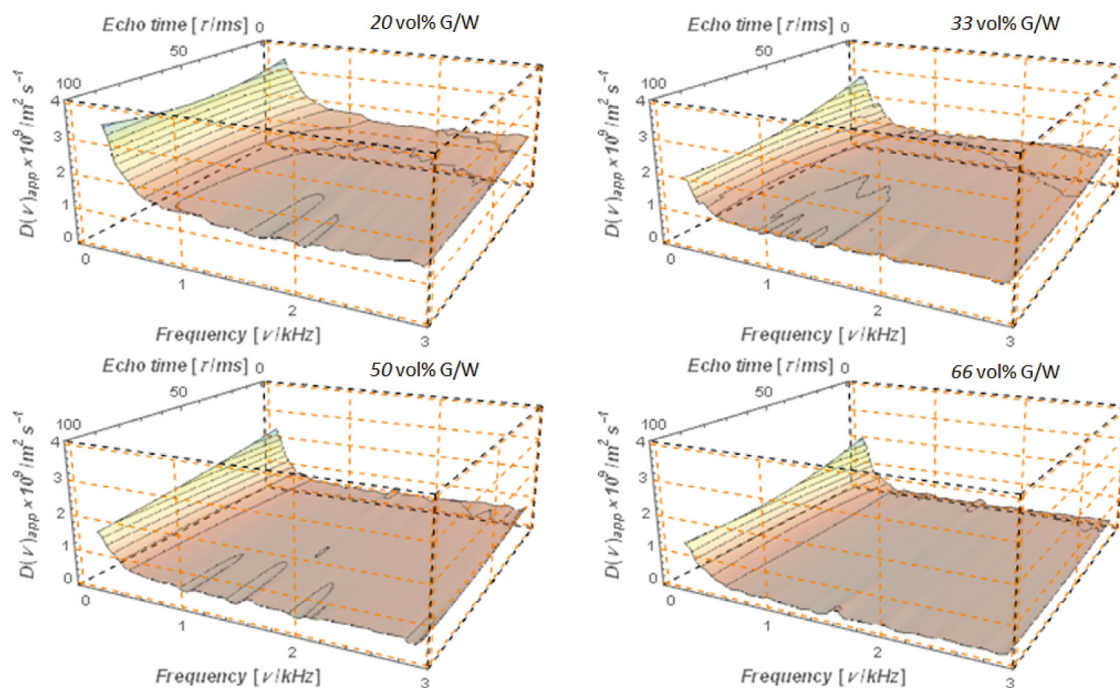
Fig. 5. 3D temporal-frequency plots of apparent VAS for the G/W mixtures with 20 vol%, 33 vol%, 50 vol%, 66 vol% of glycerol.
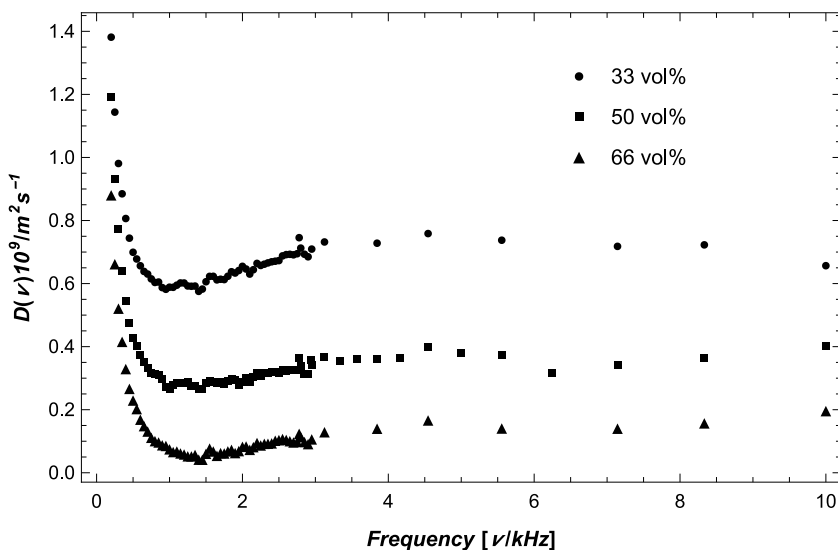

Fig. 6. VAS of G/W mixtures obtained by MGSE method on the 100 MHz NMR set-up (frequencies below 3 kHz) and on the 18.7 MHz NMR MOUSE (frequencies above 3 kHz) match well in the overlapping region.

In order to ensure the validity of results obtained by the high frequency NMR device, the measurements of the samples were repeated by using the 18.7 MHz NMR MOUSE device. Its strong and fixed MFG enables the measurement of samples up to about 10 kHz, but with the lower S/N ratio due to lower Larmor frequency. It also does not permits the measurements of water and G/W mixtures below 1 kHz, due to excessive spin echo attenuation. Fig. 6 shows the results of measurements on both devices, which match well in the overlapping frequency range.

4.1. Water–cluster interaction

In Ref. [1–4] a formation of clusters in the G/W mixtures was explained by the energies of bonding between water molecules and between glycerol molecules, which are lower than between water and glycerol molecules. Thus, the new

spectral features of G/W mixture can be attributed to the formation of clusters around the hydrofilic glycerol molecules, and this interaction with unbound water changes molecular dynamics. The disappearance of spectral hump with the increase of glycerol content indicates the depletion of the free water basin through the formation of new clusters. We believe that there are two contributions to the mixture VAS, when measuring proton signal by MGSE method: The contribution of free water that is not in contact with the clusters, and whose content decreases with the increase of glycerol concentration, and the water that interacts with the clusters or even could exchange with the clustered water. The VAS of pure glycerol and water bounded in the clusters cannot be detected due to a slow diffusion rate [47] and the short relaxation time, and is only partially observed in Fig. 1 for the spin-echo decays in zero MFG.

At room temperatures the self-diffusion coefficient of G/W mixtures does not deviate significantly from Arrhenius's law [66], allowing to consider the molecular diffusion as the motion of particles occasionally caught in potential wells created by their neighbors. Quite commonly the molecular dynamics is described by the Langevin equations, where the effect of the environment is taken into account through the fluctuating and frictional forces. The method has been widely used in the study of structural and thermal properties of matters in different phases [67]. However, the inter-molecular interaction and the coupling to other degrees of freedom are difficult to effectively include into the description. The description of interaction between water–water, water–glycerol and glycerol–glycerol molecules with a simple Lennard-Jones potential turned out to be unsuccessful even though the potential is modified by the bifurcation of the single minimum into two or more minima [68]. However, the results of MGSE measurements in ordinary fluids [47] showed that the results can be successfully explained by Langevin equations (LE), in which we consider that molecular motion at high temperatures alters molecular interactions to such an extent that they can be approximated by harmonic interaction [69]. This means that in mutual collisions, the molecules occasionally get caught in a harmonic well, which can be described by a constant k and with a minimum at $a(t)$ between x_i and x_j locations of colliding molecules. This allows to describe the molecular dynamics by the set of coupled LE

$$m_i \frac{d^2 x_i}{dt^2} + \gamma \frac{dx_i}{dt} + k \sum_{j \neq i}^{n} (x_i - x_j - a(t)) = f_i(t) \tag{9}$$

in which the ith particle is coupled to n of its closest neighbors. Here, m_i is the particle mass, γ is the friction coefficient, and f_i is the random force. The friction and the random force represent two consequences of the same physical phenomenon and are interrelated [20]

$$\gamma(\omega) = \frac{1}{k_B T} \int_0^\infty \langle f(t) f(0) \rangle \exp(i\omega t) dt, \tag{10}$$

where k_B is the Boltzmann constant. Neglecting the fluctuation of $a(t)$ and the inertial terms of LE at low frequencies , when $\omega < k/m_i$, and assuming that all particles are subjected to the same friction $\gamma(\omega) \approx \gamma = \frac{1}{k_B T} \langle |f|^2 \rangle$, the solution gives the VAS of harmonically coupled water molecules, $D_w(\omega)$, in the form

$$D_w(\omega) = \frac{k_B T}{\gamma} \frac{n + \tau_c^2 \omega^2}{n^2 + \tau_c^2 \omega^2}. \tag{11}$$

where the correlation time is $\tau_c = \gamma/k$. At zero frequency, the Einstein diffusion coefficient, $D_w(0) = \frac{k_B T}{n\gamma}$, depends on the number of coupled molecules, while at high frequencies, $D_w(\infty) = \frac{k_B T}{\gamma}$ is the diffusion rate of molecules escaping the inter-molecular capturing. This formula provides a good fit to the VAS of pure water, glycerol and ethanol [47] as well also to the results of our measurements for the VAS of G/W mixture with 0.05 vol% glycerol shown in Fig. 4. However, $D_w(\omega)$ cannot fit to the VAS of G/W mixture with the glycerol concentrations equal to or greater than 10 vol% as shown in the same figure. In the latter case, one must consider the interactions of water with the water clustered around glycerol. With a slight exaggeration that water molecules and clusters experience the same friction, γ, that the coupling constant between small and large particles is the same k, and given that the mass of clusters is large enough that the inertial term in their Langevin equations cannot be neglected at low frequencies, i.e. $\omega \approx \gamma/M$, the solution for the system of n_w light water molecules and n_c heavy clusters gives the VAS for the water molecules interacting with clusters as

$$D_{wc}(\omega) = \frac{k_B T}{\gamma n_w} \left(\frac{(n_w - 1) \tau^2 \omega^2}{(n_c + n_w)^2 + \tau^2 \omega^2} + \frac{n_c n_w + \tau^2 \omega^2 + \left(n_w - \frac{\omega^2}{\omega_0^2}\right)^2}{(2n_c + n_w) n_c + \tau^2 \omega^2 + \frac{n_c^2 \omega^2}{\tau^2 \omega_0^4} + \left(n_w - \frac{\omega^2}{\omega_0^2}\right)^2} \right), \tag{12}$$

and the VAS for the clusters interacting with water as

$$D_{cw}(\omega) = \frac{k_B T}{\gamma n_c} \left(\frac{(n_c - 1) \tau^2 \omega^2}{\left(\frac{\omega^2}{\omega_0^2} - n_c - n_w\right)^2 + \tau^2 \omega^2} + \frac{(n_c + n_w) n_w + \tau^2 \omega^2}{(2n_c + n_w) n_c + \tau^2 \omega^2 + \frac{n_c^2 \omega^2}{\tau^2 \omega_0^4} + \left(n_w - \frac{\omega^2}{\omega_0^2}\right)^2} \right), \tag{13}$$

where $\omega_o = \sqrt{k/M}$. This may be an excessive simplification, but allows the calculation of results that serve at least qualitatively to compare with our experimental results. Fig. 4 shows a good fit of $D_{wc}(\omega)$ to the data for the VAS of mixtures with 15 vol% of glycerol, if assuming that each water molecule interacts with one of adjacent aqueous molecules and one cluster and that the interaction between clusters is neglected.
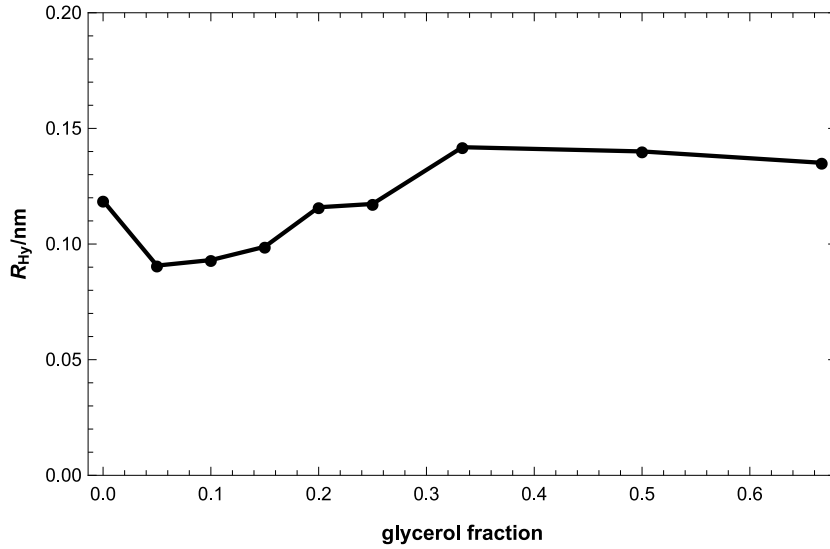
Fig. 7. The size of the hydrodynamic radius of the diffusing molecules, determined according to the SE formula, proves that only the properties of water molecules in the G/W mixture were observed.

4.2. Rate thickening of molecular friction in G/W mixture

As shown in Refs. [70,71] the self diffusion coefficient of G/W mixture decreases and the viscosity increases with decreasing temperature according the Stokes–Einstein formula (SE) in a wider range around room temperature. This formula is derived from the Einstein–Smoluchowski (ES) relation [72,73]

$$D = \frac{k_B T}{\gamma} \tag{14}$$

by relating the fluid viscosity η to the friction as $\gamma = s\pi R\eta$, which is derived from the Navier–Stokes equations for the spherical objects of radius R moving with small Reynolds numbers in a fluid. Here, the factor s depends on the boundary condition and is equal to 4 for the slip boundary condition and 6 for the stick boundaries. Thus, the hydrodynamic radius of a molecule R may be derived directly from the diffusion coefficient using the SE relation, if the viscosity of solution is known. Fig. 7 shows the dependence of water hydrodynamic radius on the glycerol content obtained by using the diffusion coefficients derived from the MGSE measurement, shown in Fig. 8, and the viscosity of G/W mixture from the Ref. [74] with the assumption of slip boundaries. The values are close to the commonly accepted radius of water, 0.14 nm [36] in the range of higher glycerol content, but slightly lower at low glycerol content, which can be attributed to the effect of hydrodynamic fluctuations.

In the generalized LE, hydrodynamic interactions and the correlation between random forces at different time are taken into account by introducing friction forces with a memory kernel, meaning that the friction acting on the particle depends on the velocity at an earlier time $\gamma(t)$ [20] giving the VAS in the form

$$D(\omega) = Re \frac{k_B T}{i\omega m + \gamma(\omega)}. \tag{15}$$

which can be considered as a generalized ES equation, in the range of low frequencies, $\omega < \gamma(\omega)/m$, or a generalized SE relation, if friction is expressed by a shear rate viscosity $\eta(\omega)$, $\gamma(\omega) = s\pi R\eta(\omega)$. Generalized SE relation was used to obtain the viscoelastic module of a complex fluid from the microscopic motion of small particles [75] in order to understanding the swimming of microorganisms, and the sedimentation in fluids. While the generalized SE gives good estimates for the motion of larger objects, its use for the molecular diffusion could lead to a systematic failure. Such models tend to severely underestimate molecular radius R from the diffusion coefficients or vice versa [76].

Since the hydrodynamic radius of small molecules is weakly dependent on the flexibility and density of the molecular structure, we still can assume the proportionality between the frequency dependent molecular friction and the shear rate viscosity in simple liquids. Thus, the inverse proportionality between the shear rate viscosity and the VAS, $\eta(\omega) \approx D(\omega)^{-1}$, reveals the shear rate thickening of viscosity of our mixtures, which appears at the glycerol contents equal to or larger than 10 vol%.

Our interpretation with the simplified LE confirms that the thickening is a consequence of water interaction with the hydro-cluster formed around glycerol molecules. It corresponds to the common understanding that the shear thickening viscosity is related to the presence of "clumps" in liquids [77].
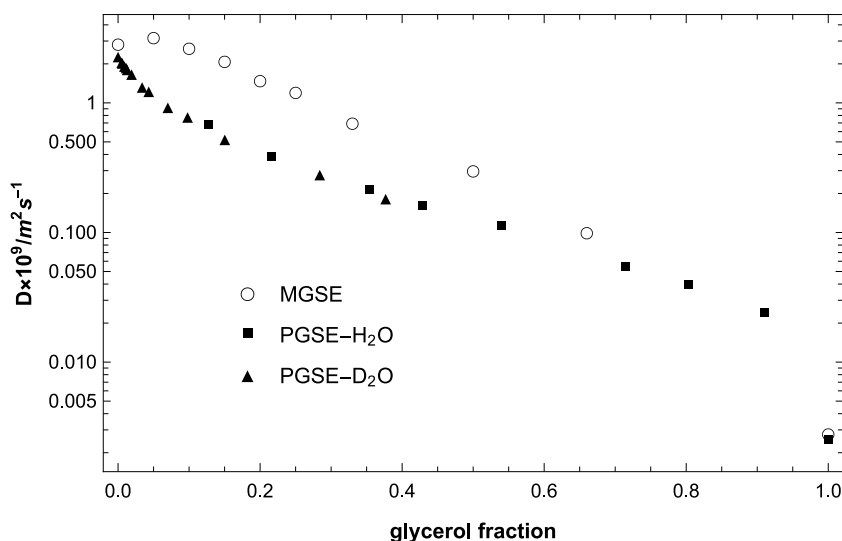
Fig. 8. The diffusion coefficient of G/W mixtures measured by our MGSE method, presented together with the results of PGSE measurements from the Ref. [13].

5. Conclusion

In Fig. 8 the diffusion coefficient obtained by the PGSE method as reported in article [13] and obtained here by MGSE method are compared. In MGSE method the VAS at the decay time $\tau = 70$ ms and at the modulation frequency $\nu = 3$ kHz is taken as a self-diffusion coefficient in order to avoid the part of spectrum with the humped surface belonging to the diffusion diversity created by the hydrodynamic fluctuations and also to be outside the low frequency spectral ridge, since its value cannot be exactly determined due to the low-frequency limit of the method. The results of both measurements match only in the cases of pure water and pure glycerol. The differences may be due to the different interpretation of spin-echo decay, given in Eq. (6) for the PGSE and Eq. (7) for the MGSE method. The article [13] does not mention the width of the MFG pulses in their experiments. This value is crucial for the correct analysis of the PGSE measurements. In addition, the differences may also appear because the proportions of glycerol, bounded and unbounded water in the hydroxyl NMR spectral line were not properly estimated in determination of water D [13]. Unlike in the PGSE method, in the processing of the MGSE spin-echo decay no calibration is required to match results of other methods, but one only needs to know the exact value of the MFG according to Eq. (7).

Study of molecular dynamics in G/W mixture by the NMR MGSE method unveils the low-frequency feature of water VAS with two indications: The small amounts of glycerol in water only partially weakens the hydrogen bonding network in water and thus increases the diffusion rate, and that the glycerol content equal or higher than 10 vol% brings about a new feature of VAS, which is the consequence of water interaction with the hydro-clusters formed around hydrophilic glycerol molecules. These interactions strongly influence the translational molecular dynamics in liquid resulting in the shear rate thickening of viscosity of water in mixtures. The shear rate thickening of viscosity alters the dynamics of other molecules if immersed in such a liquid. Instead of using the SE relation, the effect of a liquid on a submerged molecule one can treat it more correctly with the generalized EC equation, in which the friction spectrum of friction embodies the interaction of a molecule in a fluid. With this in mind, instead of the shear rate viscosity thickening, we can talk about the rate thickening of the friction coefficient in liquids, which causes an environment where rapid molecular motions and collisions are strongly inhibited.

It is well known that any protein exists as an unfolded polypeptide or random coil when translated from a sequence of mRNA to a linear chain of amino acids. Protein folding is the physical process by which a protein chain acquires its native 3-dimensional structure, a conformation that is biologically functional. A large number of experimental and simulation studies tested whether folding reactions are diffusion-controlled, whether the solvent is the source of the reaction friction, and whether the friction-dependence of folding rates generally can provide insight into folding dynamics [78,79], but these some simple questions still remain unanswered. Simulations and theory provide some insight into possible physical mechanisms of internal friction, but there are no experimental demonstrations of these ideas. An answer to this dilemma could be that in suitable solvents such as the G/W mixtures, the rate thickening of the friction coefficient dampens rapid molecular motion and collisions between molecules to create a condition for the slow process of spontaneously folding of disordered poly-peptides into biologically active protein molecules when immersed in them [80,81].

As in the cases of MGSE measurements of pure liquids [47], the VAS of G/W mixtures with the low glycerol content show a similarity of the diffusion diversity explained by the molecular self-diffusion in the vortexes of hydrodynamic

fluctuation, which disappears at higher glycerol concentrations. It can be explained that stronger molecular interactions in G/W mixtures cause faster fluctuation of hydrodynamic vortexes at a rate that cannot be observed at the shortest T intervals achieved by our device [47].

CRediT authorship contribution statement

Janez Stepišnik: Methodology, Conceptualization, Data curation, Formal analysis, Validation, Writing - original draft. **Carlos Mattea:** Data curation, Software, Methodology. **Siegfried Stapf:** Conceptualization, Funding acquisition, Resources, Supervision, Writing - review & editing. **Aleš Mohorič:** Formal analysis, Funding acquisition, Project administration, Visualization, Writing - review & editing.

References

[1] S.R. Gadre, S.D. Yeole, N. Sahu, Quantum chemical investigations on molecular clusters, Chem. Rev. 114 (2014) 12132–1217.
[2] J.H. Guo, Y. Luo, A. Augustsson, S. Kashtanov, J. Rubensson, D.K. Shuh, H. Agren, J. Nordgren, Molecular structure of alcohol-water mixtures, Phys. Rev. Lett. 91 (2003) 157401.
[3] S. Vaitheeswaran, H. Yin, J.C. Rasaiah, G. Humme, Water clusters in nonpolar cavities, Proc. Natl. Acad. Sci. USA 101 (2004) 17002–17005.
[4] R.J. Saykally, G.A. Blake, Molecular interactions and hydrogen bond tunneling dynamics: some new perspectives, Science 259 (1993) 1570–1575.
[5] J.L. Dashnau, N.V. Nucci, K.A. Sharp, J.M. Vanderkooi, Hydrogen bonding and the cryoprotective properties of glycerol/water mixtures, J. Phys. Chem. B 110 (2006) 13670–13677.
[6] J.P. Hansen, I.R. McDonald, Theory of Simple Liquids, Academic Press, London, 1986.
[7] P.M. Chaikin, T.C. Lubensky, Principles of Condensed Matter Physics, Cambridge University Press, 1995.
[8] Y. Marcus, Some thermodynamic and structural aspects of mixtures of glycerol with water, Phys. Chem. Chem. Phys 2 (2000) 4891–4896.
[9] Y. Hayashi, A. Puzenko, I. Balin, Y.E. Ryabov, Y.J. Feldman, Relaxation dynamics in glycerol-water mixtures. 2. mesoscopic feature in water rich mixtures, Phys. Chem. B 109 (2005) 9174–9177.
[10] A. Puzenko, Y. Hayashi, Y.E. Ryabov, I. Balin, Y.E. Feldman, U. Kaatze, R. Behrends, Relaxation dynamics in glycerol-water mixtures: I. glycerol-rich mixtures, Phys. Chem. B 109 (2005) 6031–6035.
[11] A. Doess, M. Paluch, H. Sillescu, G. Hinze, From strong to fragile glass formers: Secondary relaxation in polyalcohols, Phys. Rev. Lett. 88 (2002) 095701.
[12] K. Mizuno, Y. Miyashita, Y. Shindo, H. Ogawa, NMR and ft-ir studies of hydrogen bonds in ethanol-water mixtures, J. Phys. Chem. 99 (1995) 3225–3228.
[13] G. D'Errico, O. Ortona, F. Capuano, V. Vitagliano, Diffusion coefficients for the binary system glycerol + water at 25 c. a velocity correlation study, J. Chem. Eng. Data 49 (2004) 1665–1670.
[14] E. Mendelovic, L.R. Frost, T. Kloprogge, Cryogenic Raman spectroscopy of glycerol, J. Raman Spectrosc. 31 (2000) 1121–1125.
[15] C. Chen, W.Z. Li, Y.C. Song, L.D. Weng, N. Zhang, Concentration dependence of water self-diffusion coefficients in dilute glycerol–water binary and glycerol–water–sodium chloride ternary solutions and the insights from hydrogen bonds, Mol. Phys. 110 (2012) 283–291.
[16] I. Popov, A. Greenbaum-Gutina, A.P. Sokolov, Y. Feldman, The puzzling first-order phase transition in water–glycerol mixtures, Phys. Chem. Chem. Phys 17 (18063) (2015).
[17] K. Murata, H. Tanaka, Microscopic identification of the order parameter governing liquid–liquid transition in a molecular liquid, Proc. Natl. Acad. Sci. USA 112 (2015) 5956–5961.
[18] Y.Y. Efimov, Y.I. Naberukhin, The thermodynamic functions of liquid water calculated from the temperature evolution of the vibration spectrum contour, Spectrochim. Acta A 61 (2005) 1789–1794.
[19] R. Behrends, K. Fuchs, U.K.Y. Hayashi, Y. Feldman, Dielectric properties of glycerol/water mixtures at temperatures between 10 and 50 c, J. Chem. Phys 124 (2006) 144512.
[20] R. Kubo, M. Toda, N. Hashitsume, Statistical Physics II: Non-Equilibrium Statistical Mechanics, Springer-Verlag, 1991.
[21] M. Požar, B. Lovrinčevičč, L. Zoranič, T. Primorac, F. Sokolič, A. Perera, Micro-heterogeneity versus clustering in binary mixtures of ethanol with water or alkane, Phys. Chem. Chem. Phys 18 (23971) (2016).
[22] M. Sakamoto, Studies of hydrogen vibrations in transition metal hydrides by thermal neutron transmissions, J. Phys. Soc. Japan 19 (1964) 1862–1866.
[23] K.F. Larsson, Rotational and translational diffusion in complex liquids, Phys. Rev. 167 (1968) 171–182.
[24] V. Ardente, G. Nardelli, L. Reatto, Slow-neutron scattering by liquids: a hindered-translator model, Phys. Rev. 148 (1966) 124–138.
[25] G. Maret, P. Wolf, Multiple light scattering from disordered media, the effect of brownian motion of scatterers, Z. Phys. B 65 (1987) 409–423.
[26] H.E. Fischer, A.C. Barnes, P.S. Salmon, Neutron and x-ray diffraction studies of liquids and glasses, Rep. Progr. Phys. 69 (2006) 233–299.
[27] J.J. Towey, L. Dougan, Structural examination of the impact of glycerol on water structure, J. Phys. Chem. B 116 (2012) 1633–1641.
[28] R. Mills, Self-diffusion in normal and heavy water in the range 1–45°, J. Phys. Chem. 77 (1973) 685–688.
[29] Y. Nishijima, G. Oster, Diffusion in glycerol-water mixture, Bull. Chem. Soc. Japan 33 (1960) 1649–1651.
[30] D. Tomlinson, Temperature dependent self-diffusion coefficient measurement of glycerol by the pulsed NMR, Tech. Mol. Phys. 25 (1972) 735–738.
[31] E.L. Hahn, Spin-echoes, Phys. Rev. 80 (1950) 580–594.
[32] H.Y. Carr, E.M. Purcell, Effects of diffusion on free precession in nuclear magnetic resonance, Phys. Rev. 94 (1954) 630–638.
[33] H.C. Torrey, Bloch equations with diffusion terms, Phys. Rev. 104 (1956) 563–565.
[34] E.O. Stejskal, Use of spin echoes in a pulsed magnetic field gradient to study anisotropic, restricted diffusion and flow, J. Chem. Phys. 43 (1965) 3597–3603.
[35] K. Krynicki, C.D. Green, D.W. Sawyer, Pressure and temperature dependence of self-diffusion in water, Faraday Discuss. Chem. Soc. 66 (1978) 199–208.
[36] K. Yoshida, C. Waka, N. Matubayasi, M. Nakahara, A new high-temperature multinuclear-magnetic-resonance probe and the self-diffusion of light and heavy water in sub- and supercritical conditions, J. Chem. Phys. 123 (2005) 164506.
[37] F. Mallamace, M. Broccio, C. Corsaro, A. Faraone, L. Liu, C.Y. Mou, S.H. Chen, Dynamical properties of confined supercooled water: an NMR study, J. Phys.: Condens. Matter 18 (2006) S2285–2297.
[38] G. Ternström, A. Sjöstrand, G. Aly, Å. Jernqvist, Mutual diffusion coefficients of water + ethylene glycol and water + glycerol mixtures, J. Chem. Eng. Data 41 (1996) 876–879.
[39] A. Einstein, Zur Elektrodynamik bewegter Körper. (German) [On the electrodynamics of moving bodies], Ann. Phys. 322 (1905b) 891–921, http://dx.doi.org/10.1002/andp.19053221004.

[40] L.D. Landau, E.M. Lifshitz, Hydrodynamic fluctuations, J. Exp. Theor. Phys. 32 (1957) 618–619.
[41] V. Vladimirsky, J. Terletzky, Hydrodynamical theory of translational brownian motion, J. Exp. Theor. Phys. 15 (1945) 258–263.
[42] M.S. Giterman, M.E. Gertsenshtein, Theory of the brownian motion and possibilities of using it for the study of the critical state of a pure substance, J. Exp. Theor. Phys. 23 (1966) 723–728.
[43] L. Landau, E. Lifshitz, Fluid Mechanics, in: A Course of Theoretical Physics, vol. 6, Pergamon Press, Oxford, 1959.
[44] B. Alder, T. Wainright, Velocity autocorrelations for hard spheres, Phys. Rev. Lett. 18 (1967) 988–990.
[45] B. Alder, T. Wainright, Decay of the velocity autocorrelation function, Phys. Rev. A 1 (1970) 18–21.
[46] W.M. Visscher, Self-diffusion, the Green-Kubo formulas, and the long tail of the velocity-autocorrelation function, Phys. Rev. A 7 (1973) 1439–1441.
[47] J. Stepišnik, C. Mattea, S. Stapf, A. Mohorič, Molecular velocity auto-correlation of simple liquids observed by NMR MGSE method, Eur. Phys. J. B 91 (2018) 293, http://dx.doi.org/10.1140/epjb/e2018-90284-4.
[48] J. Stepišnik, I. Ardelean, Usage of internal magnetic fields to study the early hydration process of cement paste by MGSE method, J. Magn. Reson. 272 (2016) 100–107.
[49] J. Stepišnik, Analysis of NMR self-diffusion measurements by density matrix calculation, Physica B 104 (1981) 350–364.
[50] P. Callaghan, J. Stepišnik, Advances in magnetic and optical resonance, in: Warren S. Warren (Ed.), in: Generalised Analysis of Motion Using Magnetic Field Gradients, vol. 19, Academic Press, Inc, San Diego, 1996, pp. 326–389, chapter.
[51] J. Stepišnik, A new view of the spin echo diffusive diffraction in porous structures, Europhys. Lett. 60 (2002) 453–459.
[52] J. Stepišnik, G. Lahajnar, I. Zupančič, A. Mohorič, Study of translational dynamics in molten polymer by variation of gradient pulse-width of PGSE, J. Magn. Reson 236 (2013) 41–46.
[53] M. Mahoney, W. Jorgensen, Diffusion constant of the tip5p model of liquid water, J. Chem. Phys. 114 (2001) 363–366.
[54] E. Fischer, R. Kimmich, N. Fatkullin, G. Yatsenko, Segment diffusion and flip-flop spin diffusion in entangled polyethyleneoxide melts: A field-gradient NMR diffusometry study, Phys. Rev. E 62 (775) (2000).
[55] S. Meiboom, D. Gill, Modified spin-echo method for measuring nuclear relaxation times, Rev. Sci. Instrum. 29 (1958) 688–691.
[56] J. Stepišnik, Measuring and imaging of flow by NMR, Prog. Nucl. Magn. Reson. Spectrosc. 17 (1985) 187–209.
[57] P. Callaghan, J. Stepišnik, Frequency-domain analysis of spin motion using modulated gradient NMR, J. Magn. Reson. A 117 (1995) 118–122.
[58] J. Stepišnik, P. Callaghan, The long time-tail of molecular velocity correlation in a confined fluid: observation by modulated gradient spin echo NMR, Physica B 292 (2000) 296–301.
[59] P.T. Callaghan, S.L. Codd, Flow coherence in a bead pack observed using frequency domain modulated gradient nuclear magnetic resonance, Phys. Fluids 13 (2001) 421–426.
[60] D. Topgaard, C. Malmborg, O. Soederman, Restricted self-diffusion of water in a highly concentrated w/o emulsion studied using modulated gradient spin-echo NMR, J. Magn. Reson. 156 (2002) 195–201.
[61] E.C. Parsons, M.D. Does, J.C. Gore, Modified oscillating gradient pulses for direct sampling of the diffusion spectrum suitable for imaging sequences, Magn. Reson. Imaging 21 (2003) 279–285.
[62] M. Aggarwal, M. Jones, P. Calabresi, S. Mori, J. Zhang, Probing mouse brain microstructure using oscillating gradient diffusion MRI, Magn. Reson. Med. 67 (2012) 98–109, http://dx.doi.org/10.1002/mrm.22981.
[63] S. Lasič, J. Stepišnik, A. Mohorič, I. Serša, G. Planinšič, Autocorrelation spectra of an air-fluidized granular system measured by NMR, Europhys. Lett. 75 (2006) 887–893.
[64] J. Stepišnik, A. Mohorič, C. Mattea, S. Stapf, I. Serša, Velocity autocorrelation spectra in molten polymer measured by NMR modulated gradient spin-echo, Europhys. Lett. 106 (27007) (2014).
[65] B. Bluemich, F. Casanova, S. Appelt, NMR at low magnetic fields, Chem. Phys. Lett. 477 (2009) 231–240.
[66] D.C. Douglass, Self-diffusion and velocity correlation, J. Chem. Phys 35 (1961) 81–90.
[67] I. Snook, Langevin and generalised Langevin approach to the dynamics of atomic, in: Polymeric and Colloidal Systems, Gardners Books Limited, England, 2011.
[68] H. Stanley, P. Kumar, L. Xu, Z. Yan, M. Mazza, S. Buldyrev, S.H. Chen, F. Mallamace, The puzzling unsolved mysteries of liquid water: Some recent progress, Physica A 386 (2007) 729–743.
[69] A.D. Vnales, M.A. Desposito, Anomalous diffusion: Exact solution of the generalized Langevin equation for harmonically bounded particle, Phys. Rev. E 73 (2006) 016111.
[70] N.S. Cheng, Formula for the viscosity of a glycerol-water mixture, Ind. Eng. Chem. Res. 47 (2008) 3285–3288.
[71] F. Mallamace, C. Corsaro, D. Mallamace, S. Vasi, C. Vasi, H.E. Stanley, Some considerations on the transport properties of water-glycerol suspensions, J. Chem. Phys. 144 (2016) 014501.
[72] A. Einstein, Über die von der molekularkinetischen theorie der wärme geforderte bewegung von in ruhenden fluessigkeiten suspendierten teilchen, Ann. Phys. 322 (1905a) 549–560, http://dx.doi.org/10.1002/andp.19053220806.
[73] M. von Smoluchowski, Zur kinetischen theorie der brownschen molekularbewegung und der suspensionen, Ann. Phys. 326 (1906) 756–780, http://dx.doi.org/10.1002/andp.19063261405.
[74] I. Chang, H. Sillescu, Heterogeneity at the glass transition: Translational and rotational self-diffusion, J. Phys. Chem. B 101 (1997) 8794–8801.
[75] T. Mason, Estimating the viscoelastic moduli of complex fluids using generalized Stokes-Einstein equation, Rheol. Acta 39 (2000) 371–378.
[76] W.A.B. Evans, On some application of the Magnus expansion in nuclear magnetic resonance, Ann. Phys. 48 (1968) 72–93.
[77] R.G. de Kretser, S.P. Usher, P.J. Scales, D.V. Boger, K.A. Landman, Rapid filtration measurement of dewatering design and optimization parameters, AIChE J. 47 (2001) 1758–1769.
[78] M. Jacob, T. Schindler, J. Balbach, F.X. Schmid, Diffusion control in an elementary protein folding reaction, Proc. Natl. Acad. Sci. USA 94 (1997) 5622–5627.
[79] S.J. Hagen, Solvent viscosity and friction in protein folding dynamics, Curr. Protein Pept. Sci. 11 (2010) 1389–2037.
[80] R.B. Gregory, The influence of glycerol on hydrogen isotope exchange in lysozyme, Biopolymers 27 (1988) 1699–1709.
[81] Y. Wang, G. Zocchi, Viscoelastic transition and yield strain of the folded protein, PLoS One 6 (2011) e28097.