Experimental report

14/02/2017

Proposal: **9-12-440** **Council:** 4/2016

Title: Revealing the dynamics of phosphocholine molecules on SPION surface

Research area: Chemistry

This proposal is a new proposal

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Samples: $C_{26}H_{54}NO_7P$
Fe_3O_4, $C_9H_{18}=C_9H_{17}NH_2$, $C_9H_{18}=C_8H_{15}-COOH$, $C_{26}H_{54}NO_7P$

Instrument	Requested days	Allocated days	From	To
IN6	3	2	10/10/2016	12/10/2016
IN5	2	0		

Abstract:

SuperParamagnetic Iron Oxide Nanoparticles (SPIONs) contrast agents for Magnetic Resonance Imaging (MRI) technique as well as potential nanoplatforms for drug delivery. Recently we have developed a functionalization protocol based on hydrophobic interaction, which leads to the SPIONs coating with amphiphilic molecules such as, 1-octadecyl-2-hydroxy-sn-glycero-3-phosphocholine (18LPC). 18LPC/SPIONs were indeed demonstrated to be stable in water suspension and biocompatible. The interesting feature of 18LPC/SPIONs is that two layers of amphiphilic molecules, one composed by oleic acid and oleylamine (stabilizing agents during nanoparticle synthesis) and the second one composed by 18LPC, are present on the SPION surface. The dynamics of the two amphiphilic layers coating the SPIONs surface represent important variables in determining the nanoparticle stability toward aggregation processes, their interaction with biological system, such as cellular membrane, and possible complexation with small molecules such as drugs. For these reasons, here we propose to perform Quasi-Elastic Neutron Scattering (QENS) measurements on 18LPC/SPIONs using 18LPC micelle suspension as reference.

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The experiment has been performed on the TOF spectrometer IN6, using the incident wavelength λ=5.1 Å, corresponding to an energy resolution of 60-120 μeV as a function of the scattering angle and a Q range from 0.25 $Å^{-1}$ to 1.95 $Å^{-1}$.
The investigation was devoted to the study of the dynamics of the amphiphilic layers coating the surface of SuperParamagnetic Iron Oxide Nanoparticles (SPIONs), that are contrast agents for Magnetic Resonance Imaging (MRI) technique as well as potential nanoplatforms for drug delivery.

Figure 1 shows the idealized picture of the SPION nanoparticle, with the two layers of amphiphilic molecules (1-octadecyl-2-hydroxy-sn-glycero-3 phosphocholine, i.e. 18LPC).

The knowledge of the dynamics of amphiphilic molecules at the 18LPC/SPIONs surface is key to optimize both the functionalization procedure and the complexation of nanoparticles with drugs.

The 18LPC/SPIONs suspension, the 18LPC solution and the buffer alone have been measured at 3 different temperatures: 287K, 297K and 310K.

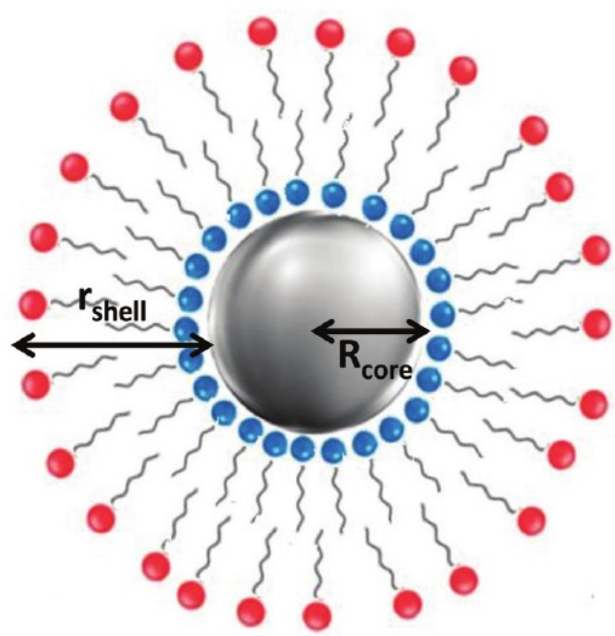

Figure 1

Before any data processing the raw spectra were corrected for empty cell contribution, self-shielding and self-absorption and normalized to a vanadium standard to take account of the not uniform detector efficiency as a function of the scattering angle. To optimize the statistics, the spectra recorded by the 337 IN6 detectors were binned into 15 constant Q spectra. Because of the high value of the transmission coefficient (t(90°) = 0.93) we decided not to correct for multiple scattering.

The signal can be modeled like this:

$$S(q,\omega) = \mathscr{R} \otimes \{ \beta \, [A_0(q)\,\mathscr{L}(\gamma,\omega) \; \ldots \\ + \; (1 - A_0(q))\,\mathscr{L}(\gamma + \Gamma,\omega)] \; \ldots \\ + \; \beta_{D_2O}\,\mathscr{L}(\gamma_{D_2O},\omega) \, \} \, . \qquad (1)$$

where $\mathscr{R}$ is the IN6 energy resolution function, while $\mathscr{L}(\gamma,\omega)$ stands for Lorenzian functions with the respective linewidth γ, describing the global roto-translational motion of nanoparticles or water molecules. On the other hand Γ is the characteristic linewidth of internal motions of the layers coating the nanoparticles. Finally, β_{D2O} is the amount of solvent signal to be subtracted from the 18LPC/SPIONs sample signal to obtain the contribution of the coated nanoparticle alone.

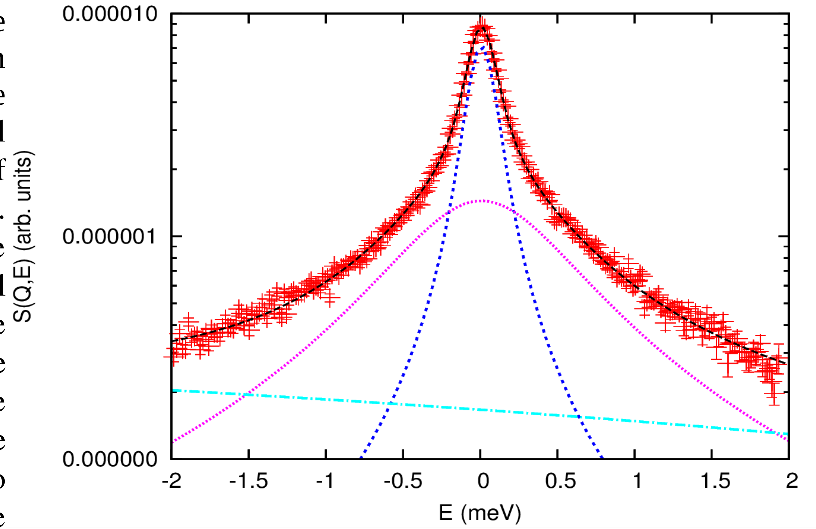

Figure 2. Signal from D_2O and fitting functions (see text for details)

To properly subtract the D_2O signal, we fitted the contribution from the solvent with two Lorentzian functions plus a background, representing global diffusion, faster relaxations and inelastic signal respectively. The result, which is reported in Figure 2 for Q=0.755 $Å^{-1}$, is very good.

Then tried to find the best way to describe the signal from 18LPC/SPIONs system, after the subtraction of the solvent contribution. In this case, the global diffusion seems to be suppressed, due to the large mass and size of the metal nanoparticles, then the spectra can be fitted by simply using an elastic peak and a Lorentzian function, representing respectively the fraction of scatterers moving too slowly to be observed by the spectrometer and the internal dynamics of the amphiphilic layers coating the SPIONs surface. In figure 3 it can be seen that also in this case the result of the fit is excellent (Q=0.755 $Å^{-1}$).

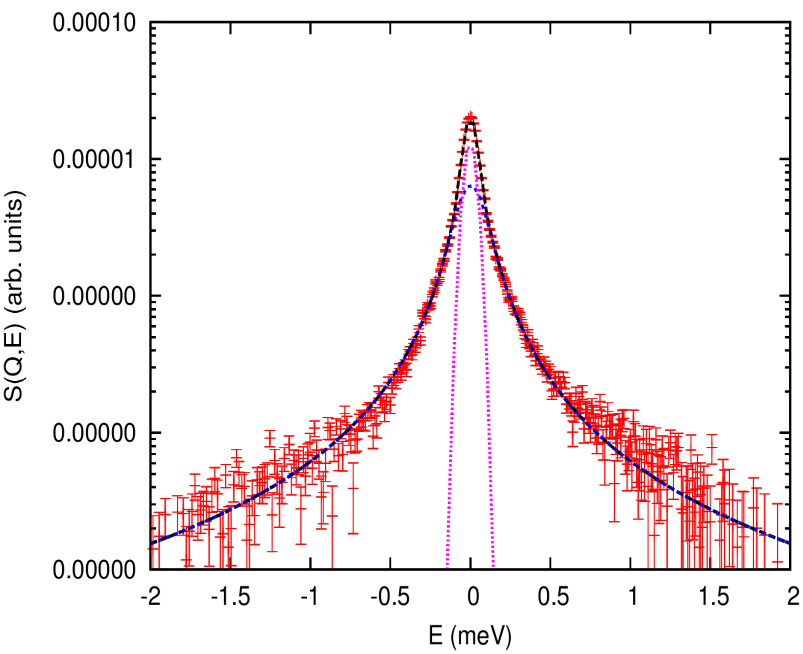

Figure 3. Signal from SPIONs and fitting functions (see text for details)

From the fitting parameters a picture emerges where the internal dynamics of the amphiphilic bilayers does not change when the temperature increases from 287K to 310K, as it can be seen from Fig. 4. Indeed, the linewidth Γ shows a T-independent trend consistent with a random jump dynamics with a characteristic time between different jumps of about 10 ps (inverse of Γ for high-Q values), possibly related to local reorientations of the 18LPC chains. The low-Q trend is also reminiscent of a confined dynamics.

Despite the similar timescale, the SPIONs samples are very different for the number of scatterers moving in the timescale observable with the IN6 accessible dynamic range. In Figure 5 we show the elastic peak intensity for the sample vs T. It can be clearly seen that the elastic peak intensity decreases as T increases, thus suggesting that a larger number of hydrogen atoms contribute to the quasielastic signal on going from 287K to 310K. The bump at 0.3 Å^{-2} is due to the residual contribution from the metal core.

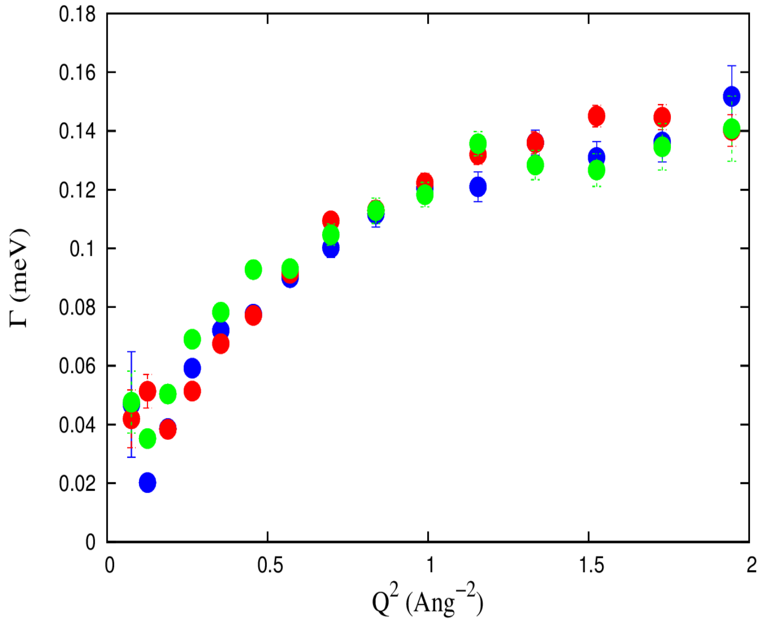

Figure 4. Green=287K, blue=297K, red=310K

The trend of the elastic intensity vs T strongly supports the need of further investigation with spectrometers allowing for better energy resolution, to access to the dynamics of amphiphilic bilayers not accessible by IN6, especially at the lowest temperatures.

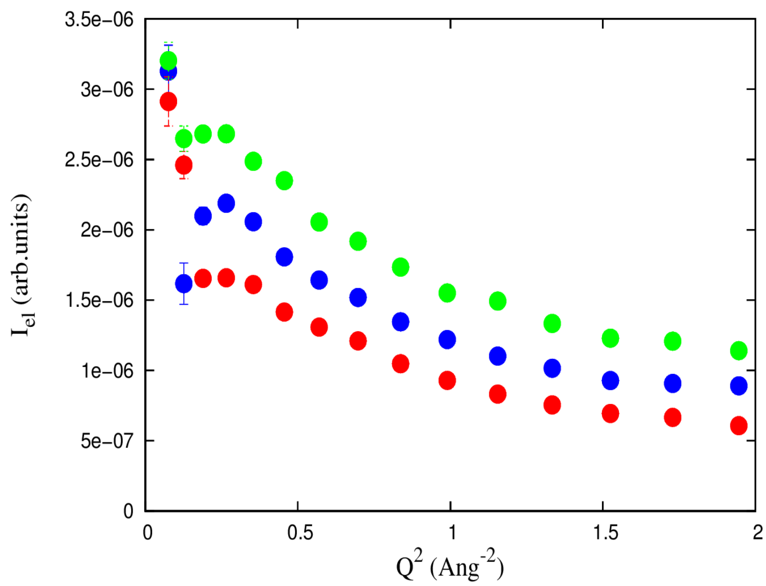

Figure 5. Green=287K, blue=297K, red=310K