ESRF	Experiment title: Interaction of Superparamagnetic Iron Oxide Nanoparticles with Supported Lipid Bilayers	Experiment number: **SC-4455**
Beamline: **ID03**	Date of experiment: from: 27/05/17 to: 31/05/17	Date of report: 20/02/18
Shifts: 12	Local contact(s): Raja Znaiguia	*Received at ESRF:*

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Report:

In the research field on nanomaterials for biomedical applications, particularly interesting are hybrid materials consisting of lipid architectures loaded with inorganic nanoparticles, where the biocompatibility of lipid-based scaffolds are combined with specific properties of nanoparticles, depending on their core composition. In this context, superparamagnetic iron oxide nanoparticles (SPIONs) are particularly relevant, to form for instance magnetoliposomes or magnetocubosomes [1, 2]. SPIONs are responsive to static and alternating magnetic fields. Thus, their responsiveness might transiently or permanently affect the structure of lipid scaffolds where they are embedded, to form responsive lipid-SPIONs hybrids, which are for instance interesting as smart vectors for drug delivery applications. Notwithstanding the promising features of lipid-SPIONs hybrids, their structural characterization and, particularly, the structural effects of static and alternating magnetic fields, are still limitedly understood [3]. The aim of the experiment sc-4455 was to elucidate the interaction of SPIONs of different nature (namely hydrophobic, with oleic acid and oleylamine coating, and hydrophilic, with a cationic coating) with 2D-lipid assemblies. i.e., supporting lipid bilayers (SLBs) of different compositions (charge and fluidity).

In Figure 1A representative XRR curves of a SLB and of the same SLB loaded with hydrophobic SPIONs and with hydrophilic cationic SPIONs are displayed, while Figure 1B, 1C shows GISAXS data of the same SLB with hydrophobic SPIONs (1B) and with hydrophilic SPIONs (1C). From the displayed data it clearly appears that a different structural effect is provoked on SLBs upon loading with hydrophobic and hydrophilic SPIONs. The same set of data were acquired with SLBs of different compositions, differing from on fluidity (DOPC, 1,2-dioleoyl-*sn*-glycero-3-phosphocholine, characterized by a fluid phase at r.t., and DPPC, 1,2-dipalmitoyl-*sn*-glycero-3-phosphocholine, characterized by a gel-like phase at r.t.) and lateral homogeneity (DOPC-DSPC (1,2-distearoyl-sn-glycero-3-phosphocholine)-cholesterol, characterized by the presence of lateral inhomogeneities, similar to raft-like domains). These data, coupled with SAXS data on liposomes of the same composition interacting with similar SPIONs, are the main object of a manuscript in preparation on the structural effect of SPIONs on lipid membranes of different fluidity, which is in preparation. In addition, the interaction between the same SPIONs was monitored with a supported lipid bilayer of biological origin [4], obtaining particularly interesting results.

After structural characterization of the interaction of SPIONs with SLBs of different composition, we monitored the responsiveness of lipid-nanoparticles assemblies to magnetic fields. In Figure 2A representative XRR data are reported of DPPC SLB in the presence of hydrophobic SPIONs before and after application of a static magnetic field. The exposure of DPPC-hydrophobic SPIONs hybrid to magnetic fields provokes a slight yet significant modification of the XRR profile. Concerning the DPPC-hydrophilic SPIONs system, a clear variation on GISAXS data are observed before (Figure 2B) and during (Figure 2C) application of a magnetic field. The variations in both XRR and GISAXS patterns upon exposure of the samples to a magnetic field unambiguously prove that the SPIONs rearrange in the lipid membrane without disrupting the overall structure of the lipid bilayer. A manuscript on the structural responsiveness of SPIONs-lipid bilayers hybrids responsiveness to magnetic fields, where the data of sc-4455 will be presented and discussed, is currently in preparation.

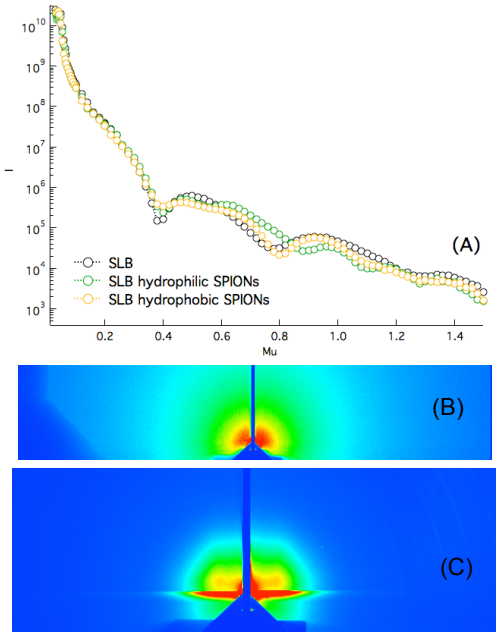

Figure 1: (A) XRR reflectivity profiles of DOPC-DSPC-cholesterol SLB in the absence and in the presence of hydrophobic and hydrophilic SPIONs; (B, C) GISAXS data of the same DOPC-DSPC-cholesterol SLB in the presence of (B) hydrophobic and (C) hydrophilic SPIONs.

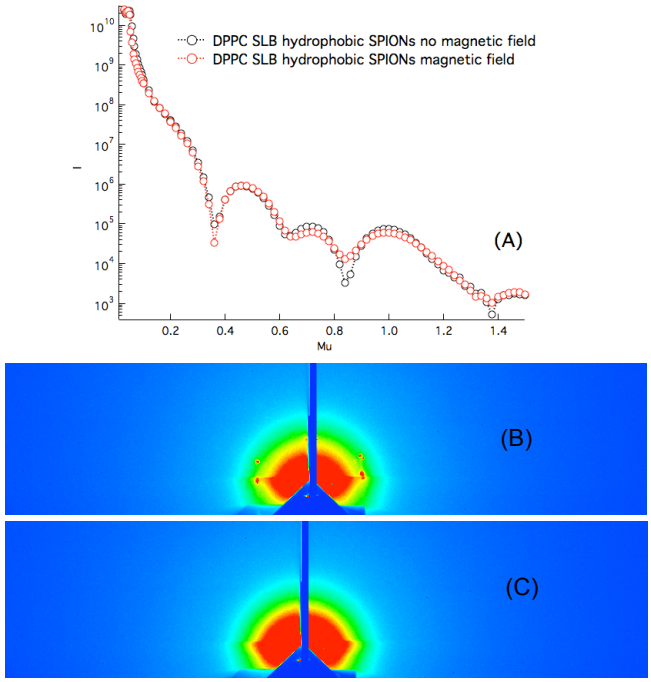

Figure 2: (A) Representative XRR curves of DPPC SLBs loaded with hydrophobic SPIONs before and during application of a magnetic field; (B, C) Representative GISAXS patterns of DPPC SLBs incubated with hydrophilic SPIONs before (B) and during (C) application of a magnetic field.

The results obtained during the experiment sc-4455 will allow significantly improve the fundamental knowledge on the interaction of SPIONs with lipid membranes, both concerning the structural characterization of the SPIONs-lipid hybrids on the nanoscale and their responsiveness to magnetic fields.

References:

[1] A Salvatore, C Montis, D Berti, P Baglioni " Multifunctional magnetoliposomes for sequential controlled release " ACS nano 10 (8), 7749-7760, 2016.

[2] C Montis, B Castroflorio, M Mendozza, A Salvatore, D Berti, P Baglioni " Magnetocubosomes for the delivery and controlled release of therapeutics " Journal of colloid and interface science 449, 317-326, 2015.

[3] M. Mendozza, C. Montis, L. Caselli, M. Wolf, P. Baglioni, D. Berti "On the thermotropic and magnetotropic phase behavior of lipid liquid crystals containing magnetic nanoparticles " *Nanoscale*, 10 (7), 3480-3488, 2018

[4] C. Montis, S. Busatto, F. Valle, A. Zendrini, A. Salvatore, Y. Gerelli, D. Berti, P. Bergese “Biogenic Supported Lipid Bilayers from Nanosized Extracellular Vesicles,” 212, Advanced Biosystems accepted, DOI: 10.1002/adbi.201700200, 2018.