Experimental report

07/02/2017

Proposal: 9-13-655 **Council:** 4/2016

Title: Influence of the protein corona onthe interaction between engineerednanoparticles and model membrane system

Research area: Chemistry

This proposal is a continuation of 9-13-584

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Experimental team: Loïc JOLY
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Samples: Fe3O4
serum proteins
POPC lipids (C42H82NO8P)

Instrument	Requested days	Allocated days	From	To
FIGARO	5	0		
D17	5	4	11/07/2016 03/10/2016	13/07/2016 05/10/2016

Abstract:

Engineered nanoparticles (NPs) found large application in medicine as theranostic materials for the diagnosis and therapy of many diseases. The understanding of the interactions of NPs with cell membranes is of fundamental importance both to tune the efficiency of NPs entry in the cell and limit their cytotoxicity. Neutron reflectometry (NR) is a powerful technique widely used to examine model membranes morphology and their response to different effectors. We propose the use of this tool to understand the nature of the interaction between NPs and a model of the cell membrane which consists in a lipid bilayer floating over a first monolayer grafted onto a gold substrate by means of thiolated tethering molecules, in vitro and in a relevant biological environment when NPs are in contact with proteins and form a new biological entity called protein corona NPs (PC). This model of the cell membrane was chosen since the floating bilayer has weaker interactions with the substrate and is free to fluctuate.

Experiment N°9-13-655 **Instrument:** D17 **Dates:** 11-13/07/2016 03-05/10/2016

Influence of the protein corona on the interaction between engineered nanoparticles and model membrane system.

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Experimental. Carboxylated Fe_3O_4 NPs were prepared according to *Sun et al.*[1] and coated by poly(maleic-anhydride-alt-ocatdecene). PEGylation was achieved using jeffamine 2000 (NHS-PEG) EDC. Lyophilized FBS was purchased from Sigma Aldrich. HC NPs were obtained according to *Di Silvio et al.*[2]. SLBs were formed by vesicle fusion using a solution of 0.5 mg/mL of DOPC liposomes. Lipid floating bilayers made of a first DSPC supported bilayer on top of which a DMPC bilayer was deposited were formed using Langmuir-Blodgett and Langmuir-Schaefer deposition . Both model membrane systems were characterized in 4 contrasts (D2O, 4MW, SMW and H2O). Experiments were carried out at 37°C. Motofit plugin for Igor Pro was used to fit the data.

First results. As in can be seen on figure 1. SLBs appeared to be poorly sensitive to the interaction with nanoparticles (Carboxylated or PEGylated), on the other hand floating DMPC bilayers appeared to have better sensitivity. However the floating bilayer was too fragile and was often destroyed during the exchange of contrast or during the injection of nanoparticles.

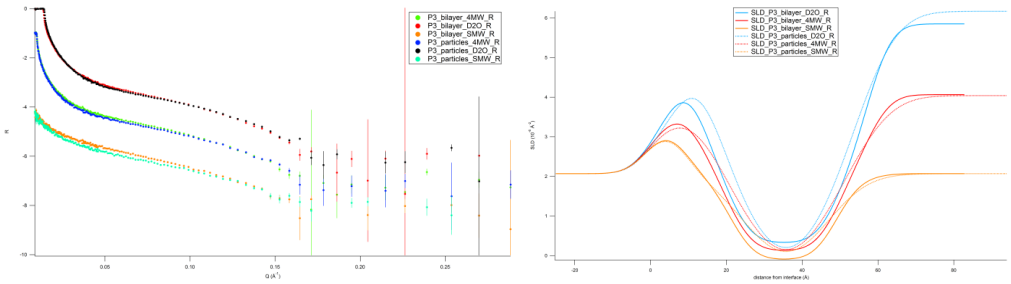

Figure 1. *Left: Reflectivity profiles of a DOPC supported bilayer before and after injection of nanoparticles. Right: Corresponding SLD profiles*

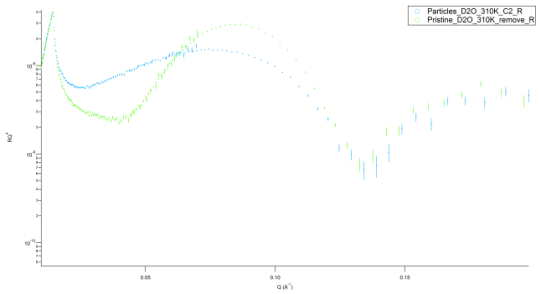

Figure 2. *Reflectivity profile in D2O of a floating bilayer before and after injection of nanoparticles. The profile after injection of particles (blue curve) is characteristic of a supported bilayer suggesting that the floating bilayer was destroyed.*

[1] Sun, S.; Zeng, H.; Robinson, D. B.; Raoux, S.; Rice, P. M.; Wang, S. X.; Li, G. *Journal of the American Chemical Society* **2003**, *126*, 273

[2] Di Silvio, D.; Rigby, N.; Bajka, B; Mayes, A.; Mackie, A; Baldelli Bombelli F.; *Nanoscale* **2015**, *7*, 11980.