Experimental report

31/08/2026

Proposal: 9-13-1161 **Council:** 10/2024

Title: Understanding the interaction of single chain nanoparticles with biomimetic model membranes.

Research area: Soft condensed matter

This proposal is a new proposal

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Samples: DOPC, cholesterol, DOPS and P(NIPAM-co-AEMA)

Instrument	Requested days	Allocated days	From	To
D17	3	0		
FIGARO	3	2	04/09/2025	06/09/2025

Abstract:

Single-chain nanoparticles (SCNPs) are ultra-small soft nano-objects formed by the intra-molecular folding of polymer chains. Amphiphilic copolymers with 2-acetoacetoxy ethyl methacrylate (AEMA) and N-isopropyl acrylamide (NIPAM) can self-fold into SCNPs with a globular structure, featuring a hydrophobic core and hydrophilic shell. These SCNPs are responsive to temperature and pH, making them promising for drug delivery. However, their interactions with biomimetic model membranes are not well understood. This study investigates P(NIPAM-co-AEMA) SCNPs (PNIPA) as drug delivery systems, focusing on their interaction with various membrane compositions to mimic real conditions and assess temperature effects. We will use neutron reflectometry (NR) to analyze the SCNPs' density profiles at solid/liquid interfaces and compare results with previous data from quartz crystal microbalance (QCM), atomic force microscopy (AFM), and NR.

Understanding the interaction of single chain nanoparticles with biomimetic model membranes

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Objectives: The main objective of this proposal was to evaluate the out-of-plane density profile of SCNPs at the solid/liquid interfaces as a function of temperature and membrane composition, in order to study their interaction with biomimetic model membranes.

Results: Measurements were performed over a full-Q range on lipid bilayers of different compositions (DOPC and DOPC: Cholesterol) to evaluate the effects of temperature and partial deuteration of the SCNPs on their membrane distribution. During the beamtime, we investigated the interaction of PNIPA SCNPs with solid supported lipid bilayer at 20 and 40°C. 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC) liposomes were assembled into a bilayer on the Silicon crystal and later SCNPs were flown over the bilayer. Excess SCNPs were then removed by rinsing with fresh water, and NR measurements were performed at each step. The experiment was repeated in three different solvents: Water, D_2O and Silicon Matched Water (38% D2O).

Figure 1 presents the neutron reflectivity curves obtained for the different systems investigated. Differences in the interaction of the unloaded SCNPs were observed between 20 and 40 °C (Figure 1A and 1B), suggesting a temperature-dependent behavior. Changes were also observed at 40 °C when luminol is encapsulated in the SCNPs (Figure 1C and 1D), which may indicate structural changes or possible release of the encapsulated luminol under certain conditions, although further analysis is required to confirm this hypothesis. Furthermore, subtle differences are observed when the degree of SCNPs deuteration and the lipid membrane composition are varied (Figure 1E and 1F), suggesting that these parameters have a more limited effect on the membrane interaction.

By fitting NR profiles obtained from three isotopic contrasts, both the bilayer structure and the presence of SCNPs were determined along the membrane’s perpendicular axis. At this stage, the

analysis was limited to hydrogenated SCNPs interacting with DOPC bilayers at 20 and 40 °C, while the remaining datasets are still pending analysis.

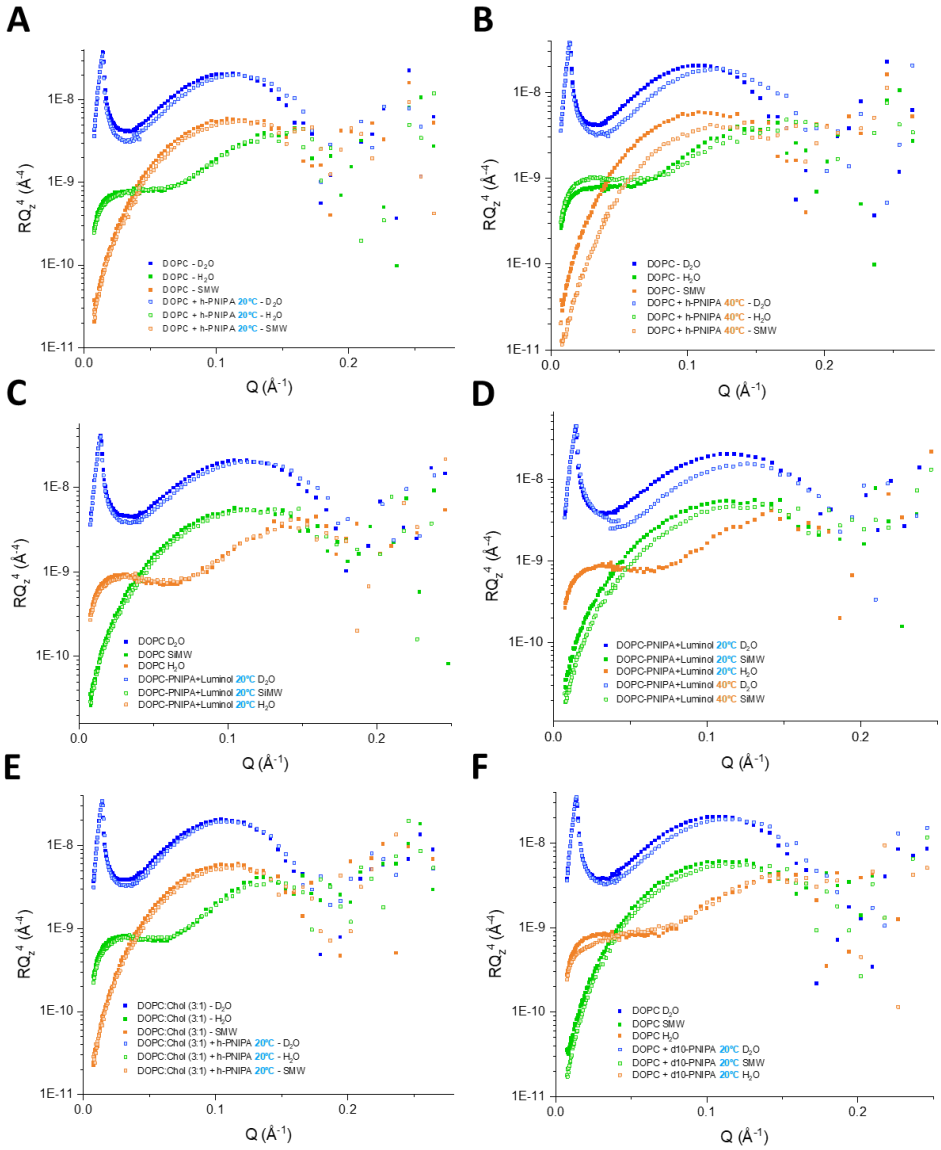

Figure 1. Neutron reflectivity curves for DOPC bilayers in contact with hydrogenated SCNPs below (A) and above (B) the LCST. Neutron reflectivity curves for DOPC bilayers in contact with hydrogenated SCNPs encapsulating luminol below (C) and above (D) the LCST. Neutron reflectivity curves for DOPC:Cholesterol (3:1) bilayers in contact with hydrogenated SCNPs (E) and deuterated (F) SCNPs with DOPC bilayers.

From these fitted parameters, the volume fraction profiles of the individual bilayer components were reconstructed, representing the relative abundance of each component as a function of the distance normal to the membrane. These distributions provide a visual representation of the membrane architecture and reveal the spatial localization of both the lipid components and the incorporated SCNPs.

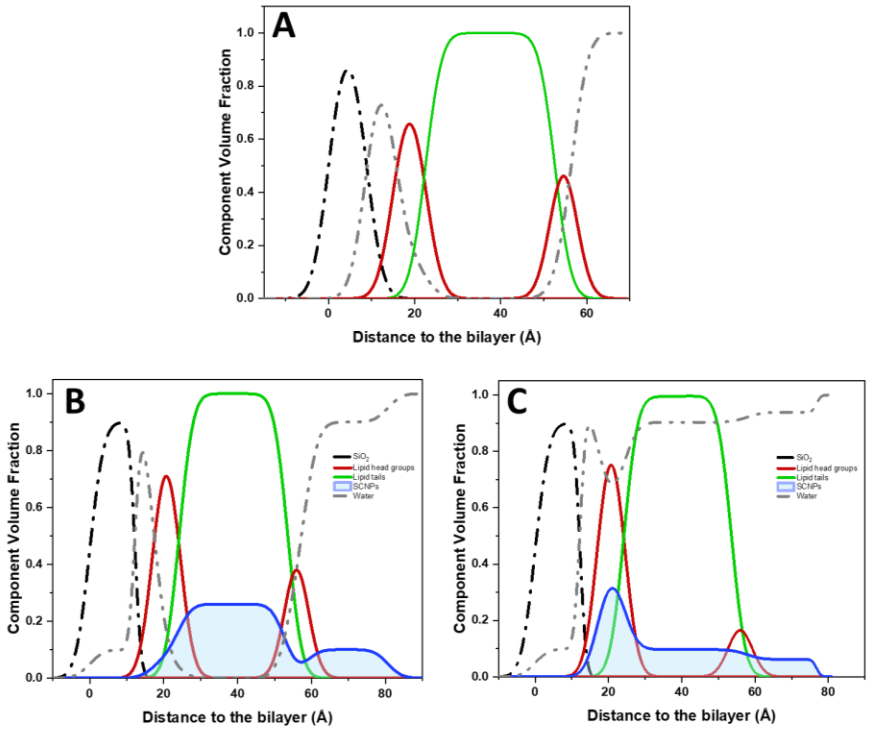

Figure 2. Component volume fraction profiles obtained from the neutron reflectometry fits for the DOPC lipid bilayer alone (A) and in the presence of hydrogenated SCNPs below (B) and above (C) the LCST.

The resulting volume fraction distributions of the bilayer components is shown in Figure 2. Prior to SCNPs incorporation, NR characterization indicated a symmetric DOPC bilayer (Figure 2A). Following incubation with hydrogenated SCNPs at 20 °C (Figure 2B), the volume fraction profile revealed that the SCNPs were predominantly localized within the hydrophobic tail region of the membrane, with only a minor fraction associated with the polar head groups. In contrast, at 40 °C (Figure 2C) the SCNPs distribution changed substantially, showing a redistribution in membrane insertion. This behavior is consistent with the temperature-responsive nature of the SCNPs, which undergo structural rearrangement above their lower critical solution temperature.

However, when the membrane structure is modified, a smaller change in the reflectometry profile is observed, which may be related to the increased membrane rigidity induced by cholesterol. Similarly, partially deuterated SCNPs showed a weaker response, potentially due to their higher hydrophilicity and water solubility compared with their hydrogenated counterparts. Nevertheless, these results are still pending fitting to determine corresponding structural changes and SCNPs-membrane interactions.

Conclusions: Overall, the results show that SCNP–membrane interactions are influenced by both nanoparticle and membrane properties. The NR data suggest a temperature-dependent redistribution of SCNPs within the membrane, supporting their potential for tunable membrane interactions and controlled cargo release.