Interaction and Integration of Amphiphilic Single-Chain Nanoparticles into Lipid Model Membranes

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Single-chain nanoparticles (SCNPs) are ultrasmall polymeric nano-objects formed by the intramolecular folding of individual polymer chains.[1] Amphiphilic copolymers of 2-acetoacetoxyethyl methacrylate (AEMA) and *N*-isopropylacrylamide (NIPAM) form SCNPs that adopt a core–shell morphology in aqueous media, with a hydrophobic core and a thermoresponsive hydrophilic corona whose conformation can be tuned by temperature and pH.[2] Their capacity to encapsulate therapeutic molecules, such as peptides, makes them attractive drug delivery candidates.[3] However, experimental insight into how SCNPs interact with and permeate lipid membranes remains scarce, with most existing studies limited to Monte Carlo simulations.[4] In this work, we experimentally investigated the interaction and integration of amphiphilic SCNPs into lipid bilayers by combining neutron scattering with confocal microscopy. Amphiphilic random copolymers were synthesized via RAFT polymerization, and SCNP formation was verified by small-angle X-ray scattering and dynamic light scattering. Neutron reflectometry (NR) on solid-supported 1,2-dioleoyl-sn-glycero-3-phosphocholine (DOPC) bilayers demonstrated the incorporation of SCNPs into the lipid membrane (Figure 1A). Confocal microscopy on giant unilamellar vesicles (GUVs), labelled with Texas Red-DHPE, further confirmed that fluorescein-tagged SCNPs translocate across the lipid membrane (Figure 1B). These findings demonstrate that amphiphilic SCNPs can integrate into lipid bilayers, highlighting their potential for drug delivery applications. This behaviour is relevant not only for controlled membrane permeation in nanomedicine but also for targeted drug release.

Keywords:
Single-chain nanoparticles, amphiphilic copolymers, lipid bilayers, membrane translocation, neutron reflectometry, drug delivery

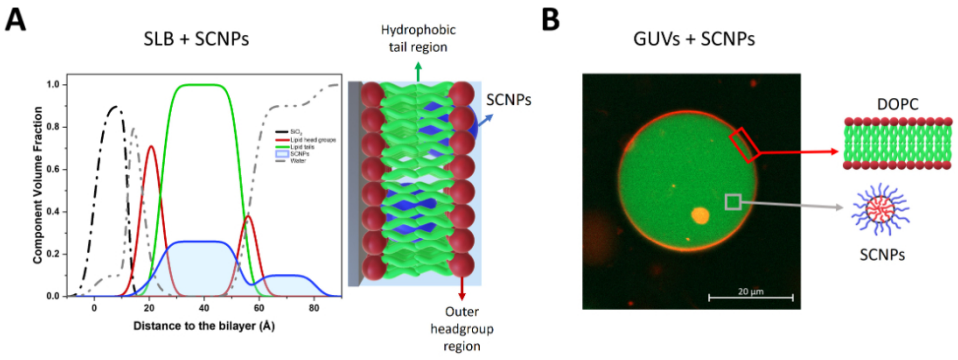

Figure 1. A) Volume fraction profile (VFP) of SCNPs interacting with a DOPC SLB derived from NR data (left) and schematic illustration of the VFP (right). B) Confocal microscopy image showing translocation of SCNPs (green) across GUV membranes (red). Scale bar: 20 µm.

References:

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