Experimental report

16/10/2020

Proposal: **9-12-578** **Council:** 4/2019

Title: Stepwise encapsulation of magneticnanoparticles into amphiphilic block copolymer vesicles through controlled water dialysis

Research area: Soft condensed matter

This proposal is a resubmission of 9-12-555

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Samples:
polydimethylsiloxane-block-polyethylene
poly(L-benzyl glutamate)-block-PEO
maghemite iron oxide (surfactant coated)

Instrument	Requested days	Allocated days	From	To
D22	3	3	10/02/2020	13/02/2020

Abstract:

Block copolymer self-assembly is a non-equilibrium process in most experimental conditions used today. In contrast, the controlled water dialysis of block copolymer solution in non-selective solvent against water affords copolymer structures at thermodynamic equilibrium. We propose to investigate the stepwise encapsulation of hydrophobic coated magnetic nanoparticles into block copolymer vesicles/micelles with the help of a controlled water dialysis pathway recently developed by the D22 team. It is hypothesized that nanoparticles can influence the pathway to the formation of polymer vesicles. The proposal aims at providing new insights into the formulation of various copolymer self-assemblies used as contrast agents for MRI applications.

Experimental Report

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Research Area: soft condensed matter

Main proposer: SANDRE Olivier

Experimental team:
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Samples : PDMS-PEO and PS-PEO copolymers, magnetic nanoparticles

Instrument	Req. Days	All. Days	From	To
D22	3	3	10/02/20	13/02/20

The solution self-assembly of amphiphilic block copolymers (BCs) rarely proceeds under equilibrium conditions conversely to surfactants. A common method to approach equilibrium conditions consists in dissolving BC macromolecules in a water-miscible solvent that is not selective for any of the two blocks and then slowly dialyzing the BC solution against water to activate hydrophobic forces and trigger the driving force of self-assembly. The dialysis cell developed at ILL (Figure 1.a) allows both to achieve the BC self-assembly close to equilibrium and to monitor the various morphological changes occurring in the solution. Contrary to recent works of TR-SANS at the 1 ms on kinetically frozen micelles (eg Kalkowski at al Macromolecules 2019, 52, 3151), this study deals on long-term kinetics using low Tg copolymers that can sustain significant rearrangements of the self-assembled objects.

Here the BCs contain a hydrophobic block (PDMS) in rubbery state at RT and a hydrophilic block (PEO) for which water is in between theta and good solvent (depending on temperature and salinity). The self-assembly has been monitored, with the BC solution in deuterated THF-d8 in the cell and heavy water in the reservoir (Figure 1.b), therefore neutron SLD contrast is on hydrogenated polymers. Two membrane porosities was varied (10kDa and 100kDa) to study to diffusion rates from/toward the cell and monitored trough conductivity in the aqueous phase (Figure 1.c). Consequently, the self-assembly kinetics was studied, as shown on Figure 1.d by plotting the SANS curves of $PDMS_{23}$-*b*-PEO_{13} as a function of the dialysis time. Data were adequately fitted by considering a transition from unimers and micelles to worm-like micelles and finally to vesicles and/or disks (Figure 1.d). Cryo-TEM analyses are currently performed at ICS (Strasbourg, M. Schmutz) to better evidence the morphologies obtained at various dialysis times.

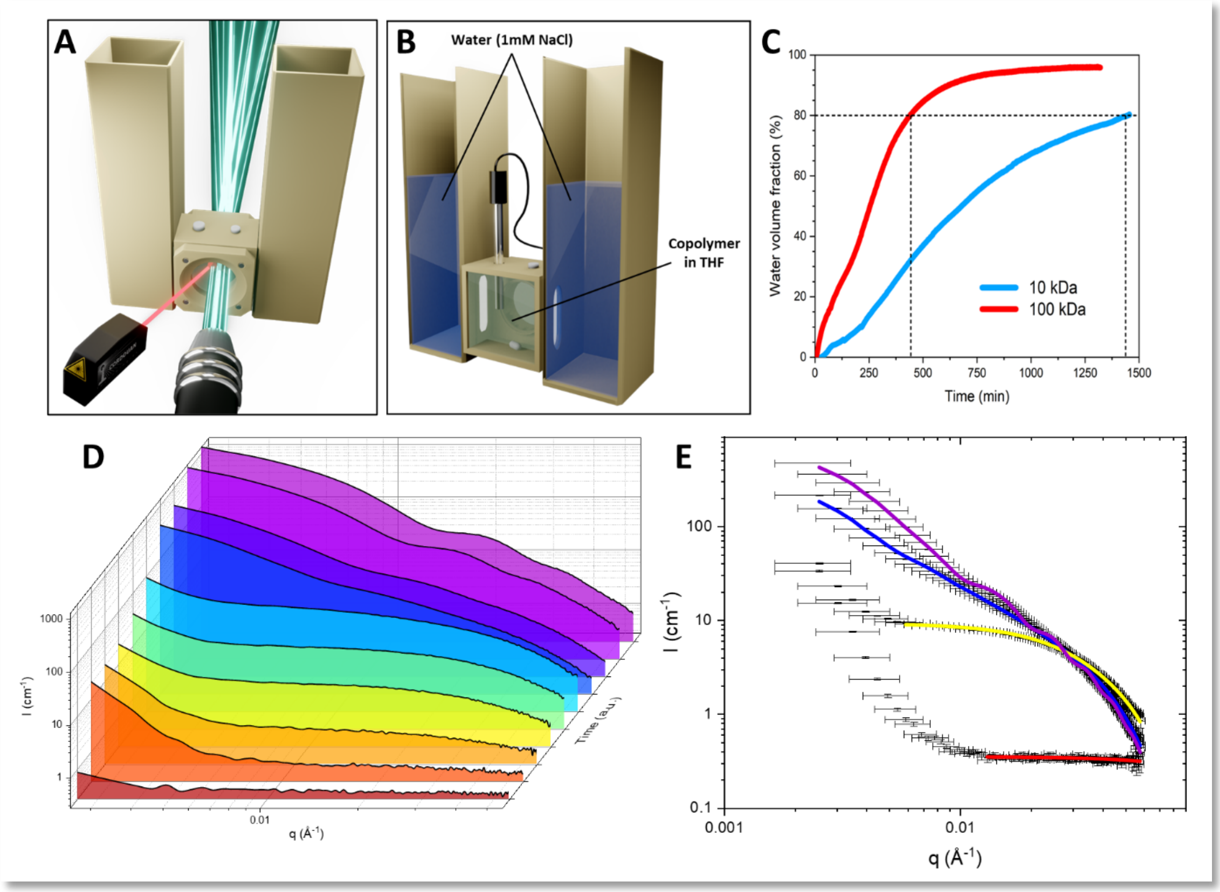

Figure 1. A- Dialysis cell used on D22 to monitor the step-by step formation of Block Copolymer (BC) vesicles. A remote-head DLS set-up could be used as well. **B-** The 4 ml cell containing the non-interacting BCs in d8-THF is sandwiched between two D_2O reservoirs containing 1 mM NaCl in order to continuously monitor the cell conductivity and then the exact water

content. Dialysis occurs through two thick regenerated cellulose membranes (10 KDa or 100 KDa cut-off). **C-** The membrane pore size is used to control the water diffusion rate and then the dialysis kinetics. **D-** Scattering curves of the PDMS$_{23}$-*b*-PEO$_{13}$ BCs self-assembly through dialysis. **E-** Typical scattering curves corresponding to the different morphologies obtained during the self-assembly of PDMS$_{23}$-*b*-PEO$_{13}$ BCs. Stage 1: statistical coils (unimers) in solution (red). Stage 2: coils + elongated rods (yellow). Stage 3: elongated rods + disks (blue). Stage 4: disks and/or vesicles (purple).

Furthermore, the BC self-assembly was performed in the presence of ultrasmall superparamagnetic iron oxide nanoparticles (USPIOs) with the aim to elucidate their location within the final structures. For this purpose, USPIOs coated with PDMS chains (according to Fresnais et col, *Appl. Sci.* 2012, 2, 485) were mixed with the PDMS-*b*-PEO BCs in THF-d$_8$ prior to the dialysis step, as previously. During the BC self-assembly, the USPIOs were expected to segregate into the forming hydrophobic domains and finally to be embedded within the vesicle membranes. The BC scattering curves with or without the presence of USPIOs are plotted in Figure 2 (A and B). The Scattering Length Density (SLD) of both USPIOs and D$_2$O being close, the contribution of the BCs only is then seen by SANS, allowing to understand how insertion of PDMS-coated USPIOs affects the self-assembly process. The continuous increase in the scattered intensity emphasizes that BC self-assembly took place in both cases (Figure 2.C). However the presence of USPIOs slows down the kinetics of self-assembly, resulting likely from a first coating step of the USPIOs by the BC, inducing retardation of the BC self-assembly. The last scattering curves for each system are plotted (Figure 2.D.). The data were fitted by membrane form factors of thickness about 9 nm in both cases, as deduced from Kratky-Porod plots. Compared to the pure copolymer, the main effect of the co-assembly with magnetic nanoparticles was a slight increase of radius-dispersity of the vesicles, in addition to the retardation effect.

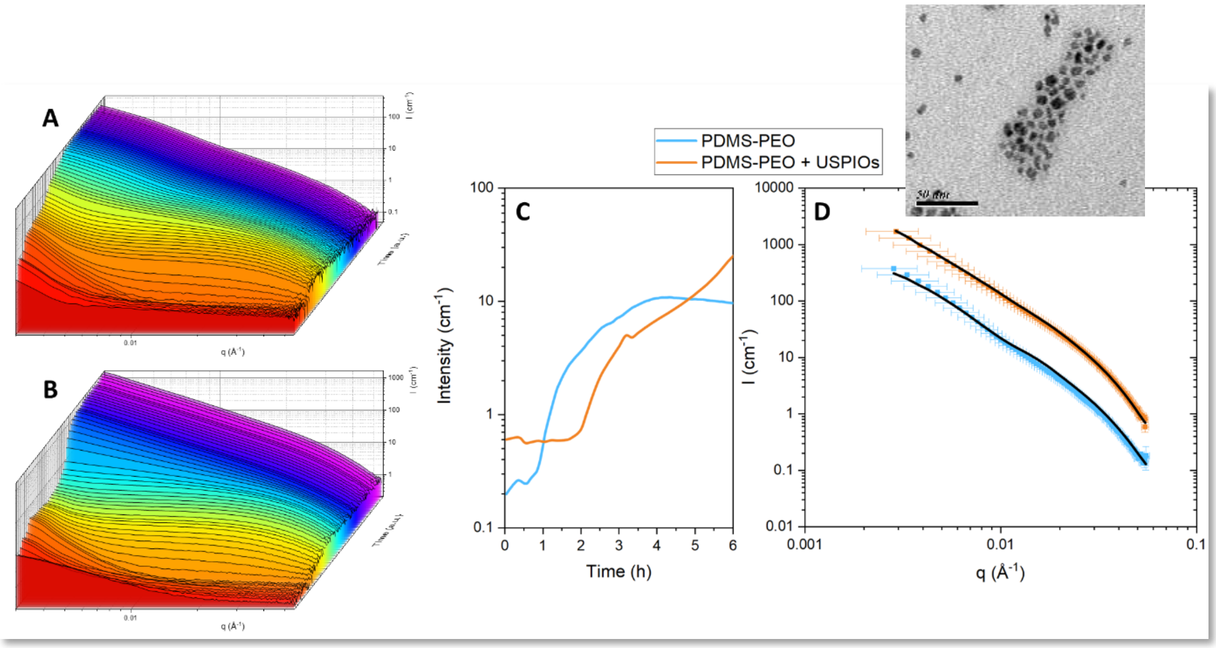

Figure 2. Scattering curves of the PDMS$_{27}$-*b*-PEO$_{17}$ BC self-assembly **A-**without **B-** with the presence of USPIOs of 6-8 nm inorganic core diameter coated by PDMS$_{80}$ chains of molar mass~6kD –viscosity 0.1 Pa·s – (23 nm hydrodynamic diameter, PDI=0.19) at a feed weight ratio (FWR) of 5 wt% (see TEM image, scale bar is 50 nm). **C-** Scattered intensity *vs.* time. **D-** Scattering curves at the final stage of the PDMS$_{27}$-*b*-PEO$_{17}$ BC self-assembly with and without presence of USPIOs. Data were fitted using either vesicle (shell) or flat disk form factors (or a combination of both).