

**Experiment title:**

Structural formation and development of framboidal vesicles

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9

**Local contact(s):**

Dr Diego Pontoni

*Received at ESRF:***Names and affiliations of applicants (\* indicates experimentalists):**

Dr. Oleksandr O. Mykhaylyk\*, University of Sheffield

Prof. Steve Armes, University of Sheffield

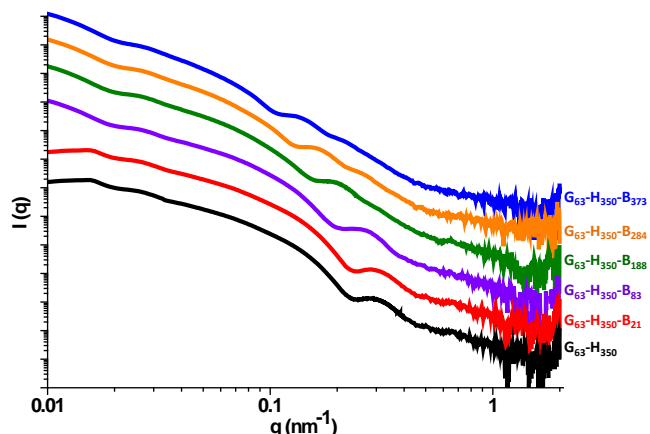
Dr Nicholas Warren\*, University of Sheffield

Dr Efrosyni Themistou, University of Sheffield

Mr David Growney\*, University of Sheffield

**Report:**

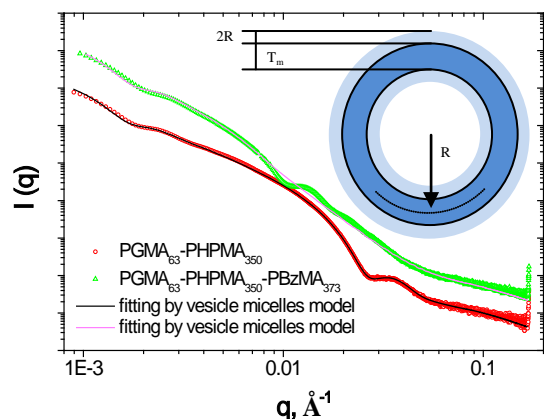
Structural evolution of framboidal poly(glycerol monomethacrylate) - poly(2-hydroxypropyl methacrylate) - poly(benzyl methacrylate) (PGMA<sub>63</sub>-PHPMA<sub>350</sub>-PBzMA<sub>x</sub>, where  $x = 0 - 373$ ) triblock copolymer vesicles during RAFT emulsion polymerization were analyzed by SAXS technique. The obtained samples corresponding to different stages of the synthesis were diluted from about 20wt% to 1wt% water solutions before the SAXS measurements. Two SAXS camera length settings (10 m and 3 m), covering  $q$ -range from  $0.01 \text{ nm}^{-1}$  to  $0.2 \text{ nm}^{-1}$ , were used for the measurements. A capillary flow through cell for liquids was used for the measurements. FReLoN Kodak 2D CCD detector was used for recordings.



**Figure 1.** Representative SAXS patterns obtained for 1wt% water solutions of linear PGMA<sub>63</sub>-PHPMA<sub>350</sub> diblock copolymer precursor vesicles and framboidal PGMA<sub>63</sub>-PHPMA<sub>350</sub>-PBzMA<sub>x</sub> (where  $x = 21, 83, 188, 284$  and  $373$ ) triblock copolymer vesicles prepared via RAFT seeded emulsion polymerisation at  $70^\circ\text{C}$ . The patterns are shifted along  $I(q)$  axis for clarity.

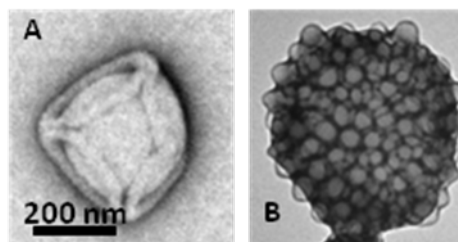
Pronounced form factor oscillations of intensities associated with vesicle membrane thickness are observed in SAXS patterns (Figure 1). Increasing amount of hydrophobic PBzMA component in the block copolymer causes shift of the form factor peaks towards small  $q$ -values indicating that the thickness of the vesicle membrane increases accordingly. The scattering form factor of block copolymer vesicles comprising a homogeneous membrane core and corona chains [1] produced a good fit to the sample corresponding to initial PGMA<sub>63</sub>-PHPMA<sub>350</sub> diblock copolymer (Figure 2, red circles). The obtained parameters were consistent with the expected self-assembled structure of vesicles (Figure 3A) composed of a homogeneous poly(2-hydroxypropyl methacrylate) membrane core and poly(glycerol monomethacrylate) corona. However, this vesicle model failed to describe scattering patterns corresponding to PGMA<sub>63</sub>-PHPMA<sub>350</sub>-PBzMA<sub>373</sub> triblock copolymers (Figure 2, green triangles) demonstrating framboidal morphology with a phase separated

membrane (Figure 3B). A poor vesicle model fit to the experimental SAXS patterns corresponding to the framboidal triblock copolymer vesicles suggests that extra structural components describing the membrane morphology should be counted in the model and, therefore, the data analysis requires a further consideration. Following the microscopy data (Figure 3B) three different approaches for the improvement of the vesicle model are currently under analysis. As one of the approaches it is assumed that the membrane core is composed of three layers and the whole membrane cross-section can be represented as PGMA corona-PHPMA-PBzMA-PHPMA-PGMA corona. Another approach is that the scattering patterns can be described by a two-population model [2] where the first population represents vesicles with a smooth membrane core surrounded by a corona and the second population represents spherical formation of poly(benzyl methacrylate) in the membrane described by a form- and structure-factor of packed spherical particles. And one more approach is based on the same two-population model where the second population is described by a form- and structure-factor of packed micelles formed by phase-separated PBzMA and PHPMA blocks.



**Figure 2.** SAXS patterns of 1wt% water solution of PGMA<sub>63</sub>-PHPMA<sub>350</sub> diblock copolymer precursor vesicles and PGMA<sub>63</sub>-PHPMA<sub>350</sub>-PBzMA<sub>373</sub> triblock copolymer framboidal vesicles (symbols) and fittings to these patterns using vesicle micelles form factor [1] (solid lines). Geometry of the vesicle micelles model is show in the graph. Fitting parameters obtained for the PGMA<sub>63</sub>-PHPMA<sub>350</sub> vesicles (black line):  $R = 1786 \text{ \AA}$ ,  $\sigma_R = 474 \text{ \AA}$  (standard deviation),  $T_m = 184 \text{ \AA}$  (thickness of the membrane core),  $\sigma_{T_m} = 26 \text{ \AA}$  (standard deviation),  $R_g = 21 \text{ \AA}$  (radius of gyration of the corona block, PGMA),  $x_{sol} = 0.55$  (solvent concentration in the membrane core).

**Figure 3.** TEM images obtained for PGMA<sub>63</sub>-PHPMA<sub>350</sub> diblock copolymer precursor vesicles (A) and PGMA<sub>63</sub>-PHPMA<sub>350</sub>-PBzMA<sub>373</sub> triblock copolymer vesicles (B) prepared by RAFT aqueous dispersion polymerisation. Note the smooth, featureless surface obtained in (A) and the distinctive framboidal morphology produced in (B).



A stopped-flow apparatus was used for the second part of our SAXS experiments to follow the dissociation of biocompatible pH-responsive amphiphilic block copolymer nanoparticles caused by the pH change (from pH 8 to pH 5) that occurs on short time scales after mixing solutions of a polymer with hydrochloric acid. The block copolymer nanoparticles were based on biocompatible hydrophilic 2-(methacryloyloxy)ethyl phosphorylcholine (MPC), pH-sensitive 2-(diisopropylamino)ethyl methacrylate (DPA) and non pH-sensitive hydrophobic 2-hydroxypropyl methacrylate (HPMA) monomers. The structural changes upon pH change in solutions of a series of pH-responsive PMPC<sub>19</sub>-*b*-PDPA<sub>900</sub> and PMPC<sub>19</sub>-*b*-P(HPMA<sub>450</sub>-*s*-DPA<sub>x</sub>) nanoparticles were tested by both time-resolved and static SAXS experiments. As a control, the non pH-sensitive PMPC<sub>19</sub>-*b*-PHPMA<sub>450</sub> block copolymer nanoparticles were also tested.

Time-resolved SAXS confirmed that the pH-responsive PMPC<sub>19</sub>-*b*-P(HPMA<sub>450</sub>-*s*-DPA<sub>450</sub>) amphiphilic block copolymer nanoparticles dissociate to unimers approximately after 3.5 seconds of mixing the polymer solution (2% w/w pH 7-8) with 0.1M hydrochloric acid solution. We are currently developing a model for SAXS analysis that will give us insights into the mechanism by which these nanoparticles dissociate to unimers.

#### References:

1. Bang, J; Jain, SM; Li, ZB; et al., Sphere, cylinder, and vesicle nanoaggregates in poly (styrene-*b*-isoprene) diblock copolymer solutions, *Macromolecules*, 2006, V39, 1199-1208.
2. Balmer, Jennifer A.; Mykhaylyk, Oleksandr O.; Schmid, Andreas; et al., Characterization of Polymer-Silica Nanocomposite Particles with Core-Shell Morphologies using Monte Carlo Simulations and Small Angle X-ray Scattering, *Langmuir*, 2011, V27, 8075-8089.