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Micellar and fractal aggregates formed by two triblock terpolymers with different arrangements of one charged, one neutral hydrophilic and one hydrophobic block

Aristeidis Papagiannopoulos [a], [*], Maria Karayianni [a], Grigoris Mountrichas [a], Stergios Pispas [a], Aurel Radulescu [b]

[a] *Theoretical and Physical Chemistry Institute, National Hellenic Research Foundation, 48 Vassileos Constantinou Avenue, 11635 Athens, Greece*
[b] *Jülich Centre for Neutron Science JCNS Forschungszentrum Jülich GmbH, Outstation at Heinz Maier-Leibnitz Zentrum (MLZ), 1 Lichtenbergstraße, 85747 Garching, Germany*

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ABSTRACT

We have studied the self-assembled structures of two triblock amphiphilic polyelectrolytes of different topologies, containing a charged poly[sodium(sulfamate/carboxylate)isoprene] (SCPI) block, a polystyrene (PS) hydrophobic block and a hydrophilic neutral poly(ethylene oxide) (PEO) block in aqueous solutions, using Small Angle Neutron Scattering (SANS) and Light Scattering (LS). SANS reveals micellar and fractal aggregates in coexistence for both systems. In the case of SCPI-b-PS-b-PEO there is a higher content in fractal aggregates in comparison with PS-b-SCPI-b-PEO. In both cases the micellar aggregates are stable under different solution conditions, whereas the fractal aggregates appear to break upon addition of salt in the PS-b-SCPI-b-PEO system. The detailed picture of the micellar aggregates is consistent with the anticipated morphology of charged and neutral spherical macromolecular brushes, extended to mixed and sequential brushes. The analytical description obtained by SANS is used to interpret the LS data which is very sensitive to the presence of two species and therefore provides information on average values of the measured parameters.

1. Introduction

Amphiphilic block copolymers, self-assembled in aqueous solutions, have been extensively studied as candidates for carriers in targeted drug delivery, bio-sensors, and tissue engineering [1]. Self-assembly of these macromolecular compounds leads to several geometries as core-shell micelles, vesicles, nanogels and aggregates depending not only on the chemistry of the monomeric units but also on external stimuli [1] as pH and salt content (for charged monomers) and temperature (for thermoresponsive blocks). Nanoparticles [2] with hydrophobic cores, and coronas made of water-soluble [3] (neutral micelles) or charged [4] macromolecular chains (polyelectrolyte micelles) provide a template for drug loading either on the hydrophobic core via hydrophobic interaction (in both cases) or via electrostatic attraction with the corona (in the case of polyelectrolyte micelles). Block copolymer topology is also influencing structure formation in such systems [5]. Charged or neutral nanogels [6] made of physically or chemically crosslinked macromolecules and polymeric aggregates [7] may also be utilized as pharmaceutical carriers.

Polyelectrolyte blocks included in self-assembled formations provide systems that can interact electrostatically with charged components in solution e.g. charged proteins or drugs. However they are highly responsive to stimuli as ionic strength and pH and in extreme cases they can be unstable [8]. On the other hand water soluble blocks are able to provide stability and solubility without the effect of ionic content. These features of the two separate systems and their individual advantages lead naturally to designing systems that combine their properties in a single system i.e. nanoformations containing both charged and neutral macromolecular blocks and to that purpose we have synthesized and studied triblock terpolymers that comprise of a hydrophobic block, a neutral water soluble block and a polyelectrolyte block in two different sequences employing anionic polymerization methodologies and

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[*] Corresponding author. Tel.: +30 210 7273825; fax: +30 210 7273794.
E-mail address: apapagiannopoulos@eie.gr (A. Papagiannopoulos).

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recently established post-polymerization functionalization reactions [9].

In this study the aggregation of two triblock terpolymers, poly [sodium(sulfamate/carboxylate) isoprene]-b-polystyrene-b-polyethylene oxide (SCPI-b-PS-b-PEO) and polystyrene-b-poly [sodium(sulfamate/carboxylate) isoprene]-b-polyethylene oxide (PS-b-SCPI-b-PEO) in aqueous solutions was investigated by scattering techniques. Under several solution conditions micellar and fractal aggregates were found to co-exist in both systems by Small Angle Neutron Scattering. Light Scattering provided average (apparent) molecular weights and sizes that were in agreement with SANS data. This investigation highlights the sensitivity of aggregation on the several types of interactions between components in solution, the effects of macromolecular architecture on the structure of the aggregates and the ability of scattering techniques to characterize in detail these complex self-assembled structures non-invasively.

2. Experimental section

2.1. Triblock terpolymers synthesis and solutions preparation

The triblock terpolymers poly[sodium(sulfamate/carboxylate) isoprene]-b-polystyrene-b-polyethylene oxide ($SCPI_{230}$-b-PS_{52}-b-PEO_{151}) from now on referred to as SCPI-b-PS-b-PEO and polystyrene-b-poly[sodium(sulfamate/carboxylate) isoprene]-b-polyethylene oxide (PS_{41}-b-$SCPI_{421}$-b-PEO_{582}) from now on referred to as PS-b-SCPI-b-PEO were synthesized by a combination of anionic polymerization and post polymerization functionalization reactions [9]. The subscripts in the blocks denote the polymerization degree of each block. The SCPI block consists of isoprene units that are randomly functionalized with hydrophilic sulfamate and carboxylate groups at a proportion of ca. 75%. It is an intrinsically flexible hydrophobic polymer that dissolves in water because of the dissociating units contained in its functionalized segments. In aqueous media SCPI has one strongly charged SO_3^- group (with Na^+ as a counter ion) and a weak acidic COO^- group which is neutralized [9] by H^+ at pH below 4.2 (Fig. 1). Briefly the synthesis of the two triblock terpolymers was accomplished [10] as described below:

SCPI-b-PS-b-PEO synthesis: The synthesis of the triblock involve the anionic polymerization of a precursor triblock and the post polymerization functionalization of the polyisoprene block. The precursor polyisoprene-block-polystyrene-block-poly(ethylene oxide) (PI-PS-PEO) block copolymer was carried out by living anionic polymerization high vacuum techniques. Initially, isoprene was polymerized in benzene at room temperature, using sec-butyl lithium as initiator. Subsequently, a small amount of THF was added, followed by the addition of styrene at room temperature. Finally, phosphazine base and ethylene oxide were added and the temperature of the reaction mixture was raised to 40 °C to polymerize the PEO block. The polymerization was terminated by addition of degassed methanol followed by two drops of concentrated HCl. At the end of each polymerization step, aliquots were isolated in order to control the success of the polymerization. During the second step, i.e. the post polymerization reaction, a predetermined amount of polymer was placed in a two-necked 100 mL round bottom flask equipped with a septum. Carefully dried diethyl ether was distilled into the flask under vacuum and the copolymer was left to dissolve overnight (final copolymer concentration was $c = 50$ mg/ml). Then, chlorosulfonyl isocyanate (CSI, from Acros) was added under N_2 dropwise, while the temperature was kept at 0 °C. The reaction of the polymer with CSI was continued for 6 h at 0 °C in dark and in a stream of N_2. It has to be noted that precipitation was observed after 1 h of reaction. An amount of NaOH solution in water/methanol (1/3) was added dropwise. The diethyl ether was evaporated in vacuum and the remaining solution was refluxed overnight under N_2. After the end of the reaction, the solvents were evaporated under vacuum and the solid was dialyzed against water.

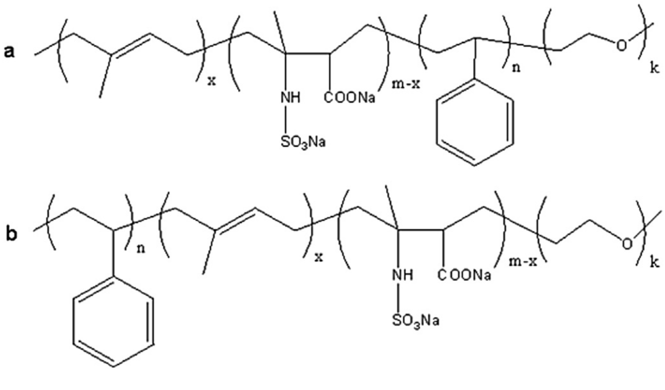

Fig. 1. Molecular structures of the two triblock terpolymers used in this study. (a) SCPI-b-PS-b-PEO and (b) PS-b-SCPI-b-PEO.

PS-b-SCPI-b-PEO synthesis: A similar, to the case of SCPI-b-PS-b-PEO, procedure has been followed for the synthesis of the precursor polymer and the post polymerization reaction. The difference was the addition order of the monomers. This time polystyrene block was synthesized first, followed by the addition of isoprene, in the absence of THF.

The copolymers were characterized by size exclusion chromatography, ^1H NMR and ATR-FTIR spectroscopy in order to determine their molecular characteristics.

In order to prepare aqueous solutions of mass concentration 1 mg/ml, 30 mg of a triblock terpolymer were stirred for 1 h in 10 ml of tetrahydrofuran (THF, from Fluka, UV spectroscopy grade) at 60 °C. Subsequently, 30 ml of D_2O or H_2O (for SANS or LS measurements respectively) was added dropwise under vigorous stirring. THF was subsequently removed by evaporation at 65 °C under stirring. NaCl was used as a salt and NaOH or HCl (NaOD or DCl in D_2O in order to minimize the incoherent scattering in SANS) for fixing the pH. The contribution of the added acid or base to the ionic strength was about 10^{-4} M hence we refer to these solutions as solutions with no added salt. All sample solutions were filtered with 0.45 μm PVDF membrane filters in order to remove any large aggregates or dust particles.

2.2. Small Angle Neutron Scattering

Small Angle Neutron Scattering (SANS) experiments were performed on the KWS-2 high intensity/wide-q small angle neutron diffractometer, at the research reactor FRM II (Jülich Centre for Neutron Science). The nominal scattering vector (q) range is from 0.002 to 0.2 $Å^{-1}$ (real space length scales ~1000 to 10 Å). This range was covered by three separate detection/neutron wavelength configurations. The high range was measured at 2 m detection length with a 4.5 Å wavelength and the intermediate and low q-ranges at 8 m detection length with 4.5 Å and 19 Å neutron wavelengths respectively.

The SANS differential cross section is obtained by the scattered intensity $I(q)$ as a function of scattering wave-vector, $q = 4\pi/\lambda sin\theta/2$, where λ is the wavelength of the neutrons and θ is the scattering angle. The scattered intensity is collected by a 2-D detector in the form of azimuthally isotropic patterns (normal for dilute solutions) which is afterwards azimuthally integrated leading to the 1-D intensity $I(q)$. The 2-D raw data are corrected for the scattering from