SELF-ORGANIZED NANOSTRUCTURES FROM NEW BLOCK CO- AND TERPOLYMERS

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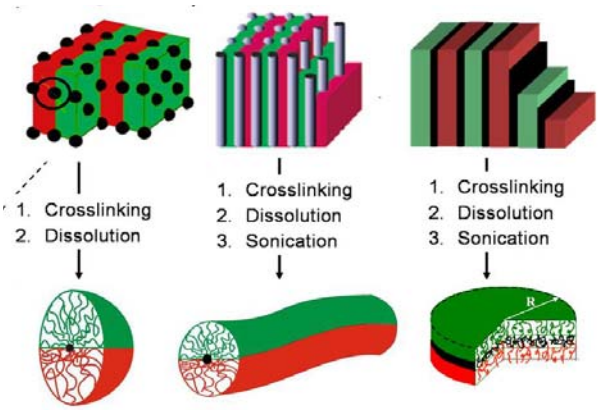
Introduction

Block co- and terpolymers can self-assemble into nanostructures in the bulk and in solution. Here, we report on new organic and hybrid, compartmentalized nanoparticles, multicompartment micelles and their interaction with other block copolymers in solution, new Janus structures, and biocompatible, clickable hybrid nanoparticles with a fluorescent silica core. These nanoparticles can combine several properties or functionalities in close proximity.

The term 'multicompartment micelles' refers to self-assembled aggregates of block copolymers with a core or corona that is further subdivided. The principal concept was introduced by Ringsdorf[1] around 10 years ago and a recent review contributes to the progress within this field of research.[2] Those structures are of great interest when it comes to the simulation or understanding of biological systems, where different functionalities in close proximity are necessary to perform distinct biological functions.[3]

Solid state nanostructures have also been successfully employed for the preparation of soluble multicompartment colloids. The strategy to obtain this goal is based on crosslinking one of the non-continuous phases of the bulk nanostructure. In our group, we have focused efforts on the preparation of Janus particles via selectively crosslinking the polybutadiene domains of polystyrene-*block*-polybutadiene-*block*-poly(methyl methacrylate) (SBM) and polystyrene-*block*-polybutadiene-*block*-poly(*tert*-butyl methacrylate) (SBT) block terpolymers.[4] The methodology is outlined in Scheme 1.

Alternatively, the hydrolytic condensation of trimethoxysilyl functions in a block copolymer can be used to crosslink particles.[5]



Scheme 1. Preparation of Janus spheres, cylinders, and discs based on the selective crosslinking of the middle block of block terpolymers.[5]

Results and Discussion

1. Block Terpolymer Micelles with a Compartmentalized Core

Using anionic polymerization, we synthesized polybutadiene-*block*-poly(2-vinylpyridine)-*block*-poly(*tert*-butyl methacrylate) (BVT, see Chart 1). These polymers form core-compartmentalized micelles in acetone solution.[6] After crosslinking of the polybutadiene (PB) core and hydrolysis of the tert-butyl ester of the poly(tert-butyl methacrylate) (PTBMA) to poly(methacrylic acid) (PMAA) they form water-soluble nanoparticles.

By quaternizing the poly(2-vinylpyridine) (P2VP) block and hydrolyzing the PtBMA block one obtains PB-P2VPq-PMAA as a polymer that forms micelles with a PB core, carrying compartments formed by an intramicellar interpolyelectrolyte complex (IPEC) of P2VPq and PMAA and a corona of excess PMAA.[7] Figure 1 shows a cryogenic transmission electron micrograph of this structure. These particles respond to pH and salinity of the solution.

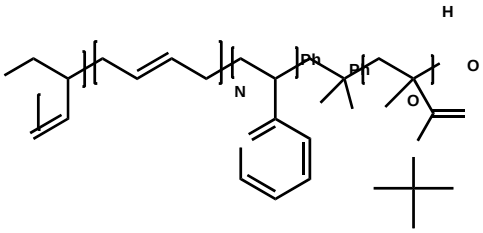


Chart 1. Structure of BVT block terpolymer

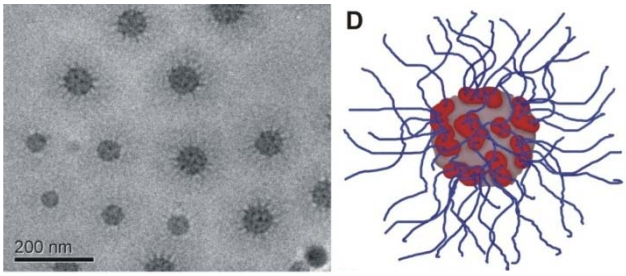


Figure 1. Cryo-TEM micrographs of $B_{800}VPq_{190}MAA_{550}$ in aqueous solution at pH 10 with proposed structure.

Interaction with a Blockcopolymer poly(ethylene oxide)-*block*-P2VPq (PEO-b-P2VPq) block copolymer leads to even more complex core-shell-shell corona structures, as depicted in Figures 2 and 3.[8]

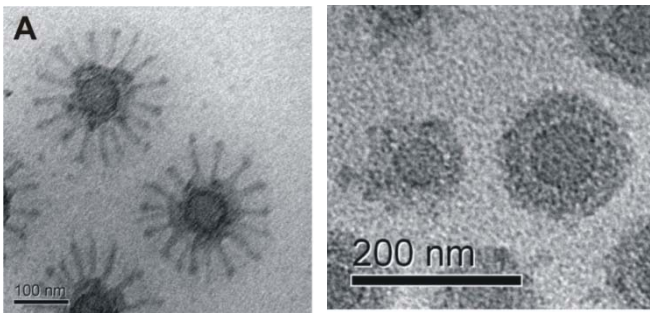


Figure 2 . Cryo-TEM micrographs IPECs of $B_{800}VPq_{190}MAA_{550}$ with $Vq_{94}EO_{1245}$. Left: after 1h, right: equilibrium structure after 10 days.

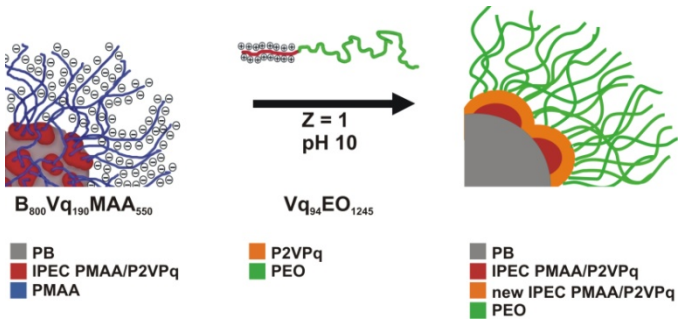
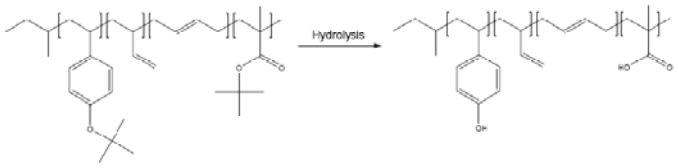


Figure 3. Formation of IPECs between negatively charged $B_{800}VPq_{190}MAA_{550}$ block terpolymer micelles and positively charged $VPq_{94}EO_{1250}$ diblock copolymers at Z(+/-) = 1

2. Janus Particles via Crosslinking of Block Terpolymers in the Bulk

To render Janus particles with more versatile functions, we synthesized a new block terpolymer by anionic polymerization, poly(*p*-*tert*-butoxystyrene)-*block*-polybutadiene-*block*-poly(*tert*-butyl methacrylate) (tSBT). Poly(*p*-*tert*-butoxystyrene) (PtS) can be hydrolyzed to poly(*p*-hydroxystyrene) (PHS), which renders the block water-soluble at pH ≥ 10.5 (Scheme 2).[9]



Scheme2. Structures of tSBT and HS-B-MAA block terpolymers

Films of $tS_{46}B_{16}T_{38}^{163}$ (the subscripts denote the weight fractions and the superscript the molecular weight in kg/mol) form a morphology with PB cylinders between lamellae of PtBS and PtBMA (lc morphology). This morphology is maintained by photocrosslinking of the PB block rendering Janus cylinders. However, after swelling in an acetonitrile/decane emulsion, crosslinking with S_2Cl_2 and sonication we did not find Janus cylinders but, for the first time, Janus ribbons (Figure 4).

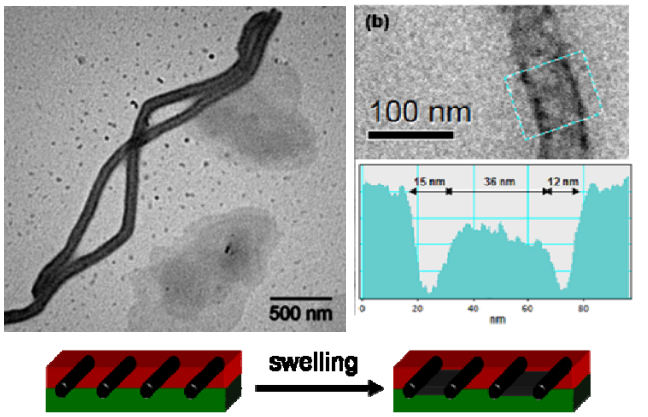


Figure 4. TEM and cryo-TEM images of Janus ribbons from tSBT block terpolymers.

The Janus cylinders can be partially or fully hydrolyzed. Figure 5 shows a partially hydrolyzed Janus cylinder at pH 11, where only PMAA is soluble whereas PtS collapses onto the PB-core. The Janus character is clearly seen.

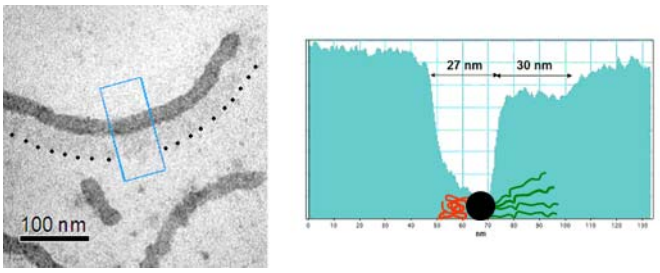
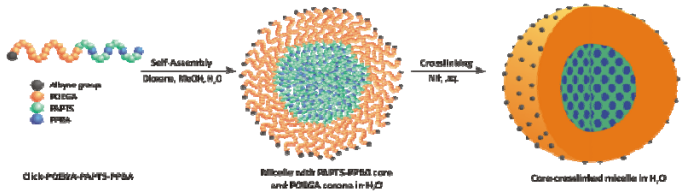


Figure 5. Cryo-TEM image and density profile of tBS-B-MAA Janus cylinders in water at pH 11. The PMAA hemisphere (dotted line) is expanded whereas the PtBS hemisphere is collapsed.

3. Biocompatible, Clickable, Fluorescent Hybrid Nanoparticles

Block copolymer of oligo(ethylene glycol) acrylate (OEGA) and (3-acryloxypropyl)trimethoxysilane (APTS) was synthesized by RAFT polymerization OEGA was chosen for polymerization of the first block because of its excellent protein repellence. Its good solubility in most common organic solvents and water guarantees good stabilization of the later aggregates in both organic solvents and water and allows for further reactions in a variety of solvents. APTS was chosen due to its ability to undergo crosslinking into a stable, inorganic silsesquioxane network under basic conditions. Additionally, 1-pyrenebutyl acrylate (PBA) was added as a comonomer in the second block (molar ratio APTS:PBA = 4:1) to introduce fluorescent tags into the hydrophobic block. It can furthermore be considered as a hydrophobic drug mimic.[10]

Self-assembly in water led to well-defined micelles which were transformed to hybrid nanoparticles by hydrolytic crosslinking of the silyl moiety using ammonia (Scheme 3). The cryo-TEM images (Figure 6) show spherical micelles with a moderate size-distribution. Consequently, the size of the micelles can be tuned by changing the length of the hydrophobic block.



Scheme 3. Preparation of clickable hybrid nanoparticles via self-assembly and crosslinking in H_2O.

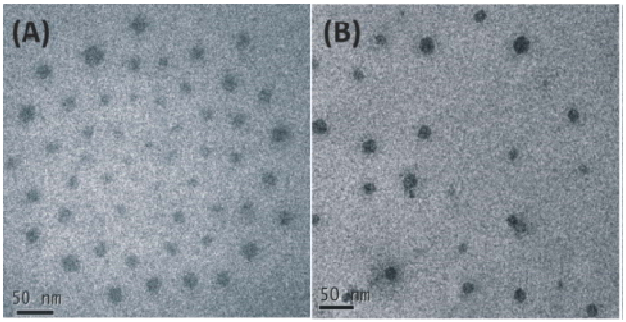


Figure 6. Cryo-TEM images of crosslinked aggregates in water (c = 0.1 g/L). The aggregates were formed out of $OEGA_{107}$-($APTS_{62}$-co-PBA_{17}) (A), and $OEGA_{107}$-(APTS80-co-PBA_{25}) (B)

Fluorescence and UV-Vis measurements give proof of the incorporation of the dye within the polymer and later aggregates. The measurements demonstrate the excellent fluorescent properties of pyrene as a biomarker.

The accessibility of the click function at the periphery of the nanoparticles was assessed via a conjugation of a second dye. The successful clicking of azido-functionalized Rhodamine B onto the nanoparticles highlights the possibility of further modifying the nanoparticles in a facile and orthogonal fashion. The click chemistry works well before and after crosslinking.

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References

1 H. Ringsdorf; P. Lehman; R. Weberskirch, Book of Abstracts, 217th ACS National Meeting Anaheim; 1999.
2 J.-F. Lutz; A. Laschewsky *Macromol. Chem. Phys.* **2005**, *206*, 813.
3 Z. Li; M. A. Hillmyer; T. Lodge *Langmuir* **2006**, *22*, 9409.
4 A. Walther, A.H.E. Müller *Soft Matter* **2008**, *4*, 663
5 J. Du, Y. Chen. *Angew. Chem.* **2004**, *116*, 5194; A. Burns, H. Ow, U. Wiesner *Chem. Soc. Rev.* **2006**, *35*, 1028.
6 F. Schacher, A. Walther, M. Ruppel, M. Drechsler, A. H. E. Müller *Macromolecules* **2009**, *42*, 3540.
7 F. Schacher, A. Walther, A. H. E. Müller *Langmuir* **2009**, *25*, 10962.
8 F Schacher, E. Betthausen, A. Walther, H. Schmalz, D. V. Pergushov, A. H. E. Müller *ACS Nano* **2009**, *3*, 2095.
9 A. Wolf, A. Walther, A.H.E. Müller, these preprints.
10 M. Müllner, A. Schallon, A. Walther, R. Freitag, A. H.E. Müller, these preprints.