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Best wishes,

Liz Dunn

Liz Dunn, Editor, *Soft Matter*

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September 14, 2014

Dear Katie:

In the end of June, you have invited me to write a Highlight article to *Soft Matter*. Now we finished it and submitted our manuscript entitled "Self-assembly of nanostructured block copolymer nanoparticles".

In this Highlight article, we have reviewed theoretical and experimental results on the topic of self-assembly of nanostructured block copolymer nanoparticles. We mainly focus on how to manipulate their hierarchical nanostructures and what kind of advantages these complex nanoparticles would bring to researchers in different fields. We hope this Highlight article will attract a broad audience from different research areas.

Soft Matters is a leading journal related to colloids and polymers. We believed that the broadest section of your readership will interest in our manuscript and we hope it will be accepted by your esteemed journal for publication.

Sincerely yours,

Dr. Zhaoxia Jin

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HIGHLIGHT

Self-assembly of nanostructured block copolymer nanoparticles

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In this highlight, we discuss the self-assembly of block copolymer (BCP) nanoparticles. We first review the state-of-art of hierarchical structural features of BCP nanoparticles due to 3D geometric confinement, both in theory and experiments. At the same time, we also highlight the applications based on these structural features: the generation of multifunctional hybrid nanoparticles, the fabrication of mesoporous BCP nanoparticles, and applications of using BCP nanoparticles as nanocontainers or nanocargos. Finally, we discuss the challenge in the fabrication and potential applications of nanostructured BCP nanoparticles.

1. Introduction

Nature demonstrates great ability to precisely control hierarchical structure of materials in different length scales. By using these structural features, it further arranges complex functional groups orderly into an integrated system, leading to its harmony of multifunctional processes. The elegant control of structure and function of materials motivates physicists, chemists and material scientists to learn the underlying mechanism. Great efforts have been done in the fabrication of inorganic systems with hierarchical structures. However, for polymer-based nanoparticles (NPs), the ability to control their structures in different length scales is still a big challenge. Because of the biocompatibility, biorecognition ability, environmentally switchable release of loading molecules, polymer-based NPs with hierarchical structures are attractive for their potential applications in biological and pharmaceutical area.[1] To this aim, the investigation of block copolymer (BCP) NPs with controllable surface pattern and internal nanostructures attracts much attention of researchers, both in theoretical and experimental studies, because the self-assembly of BCP is a powerful tool to construct various nanostructures. The richness of self-assembly of BCP can be used in designing polymer particles with extensive inner structures.[2] After more than a decade of research, now researchers have a lot of strategies in hand to delicately control the nanostructure and functions of polymer NPs, on the basis of their understanding of the self-assembly of BCP. In this highlight, we focus on the progress of cognition of BCP self-assembly and how it guides us to develop fabrication strategies of polymer NPs with predicted nanostructures and surface chemistry.

2. Theoretical studies of structural features of nanostructured block copolymer nanoparticles via self-assembly

Placing BCP under confinement introduces a number of extrinsic factors, such as commensurability and surface-polymer interactions, which strongly influence BCP nanostructures based on its intrinsic self-assembly.[3] Spatial confinement provides a powerful way to break the symmetry of an unconfined structure, showing an effective route to manipulate its self-assembled nanostructures.[4,5] A rich variety of novel structures have been revealed under confined geometries, and it could not be formed in bulk. 3D confinement of BCP, i.e. BCP nanoparticles, presents the most tightly confining geometry.[6,7] In 2003, Fraaije and Sevink first reported their study in assembly of polymer surfactants through self-consistent-field simulation (SCF).[8] They discovered remarkable patterned nanostructures, such as bicontinuous structures derived from self-assembly of amphiphilic polymer molecules. SCF theory is known to be accurate in evaluating the free energy of polymer systems in both weak and strong segregation regions.[9] Uneyama and Doi have further extended SCF theory to any blend of homopolymers and BCP of any topological structure.[10] This progress has aroused a series of researches into blends of BCP with homopolymers to create more complex inner structures based on the self-assembly of BCP and the disturbance from addition of homopolymers.[11] On the other hand, dissipative particle dynamics (DPD) approach[12] and Monte Carlo simulations[13,14] are also used in the study of microphase separation of diblock copolymers NPs. In particular, Han et al indicate that the increase of polydispersity index of diblock copolymer will cause structural change due to the frustration between phase-separation morphology in bulk and the confined spacing.[14] Shi's group have systematically studied the self-assembly of symmetric diblock copolymers confined in spherical nanopores using simulated annealing Monte Carlo simulations.[13] They observed that with surface field changing, from neutral to weakly preferential and strongly preferential to one block, the generated nanostructures change from perpendicular lamellae to helices, and/or embedded structures, and finally onion-like lamellae (Fig. 1). Moreover, the chain conformations of 3D confined structures are different from that in 2D confined situation. For cylinder-forming diblock copolymers NPs, BCP nanoparticles with center-symmetric inner structure, stacked toroids, single-, double-, triple- and quadruple- helices, saddle-related structures, coiled-cylinder structures are demonstrated through real-space SCF calculations.[15] For a blend of symmetric AB diblock copolymer and A-homopolymers, the A-homopolymers acted as filler, thus control the volume fraction of the A-component in the system, and the final obtained internal structures include curved concentric arrays, honeycomb-like (or concentric perforated lamellae), circular helices or stacked hoops and spheres. Moreover, in case of binary blends of diblock copolymer (AB) and an incompatible homopolymer (C) confined in spherical cavities, the internal morphology of the spherical polymeric particles is controlled by the volume fraction of homopolymers, the degree of confinement, and the composition of the copolymer.[16] Homopolymers may act as an additional controlling parameter of the self-assembled nanostructure. In particular, Janus-like particles with the copolymers and the homopolymers on different sides are observed. On the other hand, Cell dynamics simulation (CDS) is a fast method to simulate kinetic processes in phase separation systems of large size, and it has been used in the studies of BCP systems.[17] Pinna et al. investigated morphology of thin BCP film around a nanoparticle by using CDS.[18,19] Their simulation indicates that novel porous nanocontainers can be formed by coating a sacrificial nanobead with a BCP layer, nanostructure of which is well-controlled.[19]

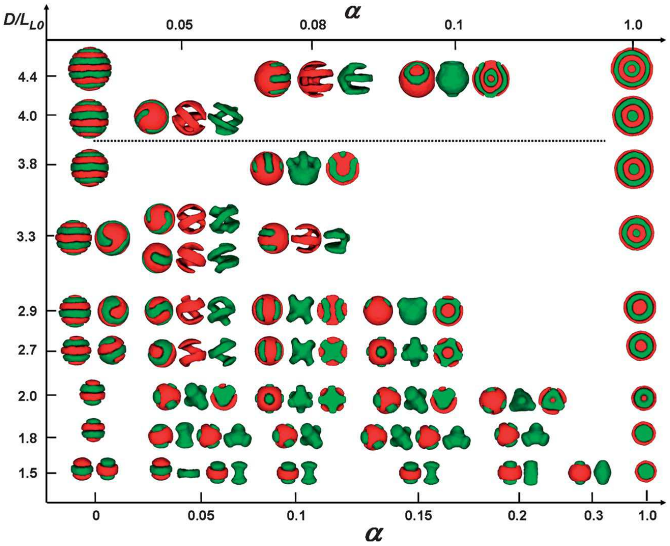

Fig. 1 Self-assembled morphologies for symmetric diblock copolymers confined in spherical pores as functions of the ratio D/L_0 and α, the strength of the surface preference for the A-block. In the figure, the morphologies are corresponding to the lower α coordinate for $D/L_0 \leq 3.8$ and corresponding to the upper α coordinate for $D/L_0 > 3.8$. Adapted with permission from ref. 13. Copyright 2007, American Chemical Society.

In addition, soft confinement is existed in the formation of polymer droplets in a solvent environment. Surface-polymer interaction is replaced by solvent-polymer interaction and it is more general for the production of polymer NPs by using emulsion or precipitation methods. Shi's group also reported how soft confinement induces morphological transformation of diblock copolymers particles which has similarity with hard confinement.[20]

Except the internal morphologies, surface pattern of BCP nanoparticles is a meaningful topic that determines patterned-arrangement of domains with different chemical properties. The particles with ordered surface pattern are named as patchy particles. Tang et al. first reported their study of the phase-separation induced surface pattern of diblock copolymers using a finite volume method.[21] Stable and intrinsic defects appear in the periodic arrangement of domains on the curved surface due to distinct Euler characteristic of the surface. Recently, Zhang et al. investigated the defect structures and ordering behaviour of lamellar and cylindrical phases of BCP confined on spherical substrates by Landau-Brazovskii theory.[22] They observed that in cylindrical case, isolated disclinations and scars are generated on the spherical substrates and the number of excess dislocations in scars linearly depends on the sphere radius; for lamellar phase, three types of defect structures (hedgehog, spiral and quasi-baseball) will appear on spherical substrates. In recent years, peoples working in theoretical simulations move their research to ABC triblock copolymers, leading the development of patchy multi-compartmental NPs.[22-24] Three blocks of copolymers provide more experimental parameters which can be used to manipulate nanostructure of polymer NPs.[23-25]

3. Experimental studies of nanostructured BCP nanoparticles

Eisenberg's group first observed novel morphologies of mesosized aggregation of asymmetric polystyrene-*b*-poly(acrylic acid) generated in solution by self-assembly.[26] They are amazed at the crystal-like aggregates morphologies. In 2001, Lu et al. first reported their fabrication of BCP microspheres with self-assembled internal structures by using emulsion method.[27] The combination of emulsification and self-assembly of BCP yields a variety of nanostructures which have not be observed before.[28] Okubo et al. reported onion-like multilayered composite particles composed of polystyrene-*b*-poly(methyl methacrylate) (PS-*b*-PMMA) or PS/PS-*b*-PMMA/PMMA, in which the weight of PS and PMMA were same.[29] Arsenault et al. first reported how 3D confinement leads to structural transformation of polystyrene-*b*-polyferrocenylethylmethylsilane (PS-*b*-PFEMS) NPs generated by using colloidal crystal as templates.[30] They further investigated the 3D confinement of lamellar and cylindrical diblock copolymer in silica colloidal and inverse colloidal crystals.[31] Surface modification alters the wetting interaction of BCP with colloidal crystal template, leading to the change of internal morphology of PS-*b*-PFEMS NPs. Similarly, silica nanobowls[32] and hemispherical cavities[33] can also be used as template to generate BCP nanoparticles with controlled size and shapes. Interfacial interaction between BCP and template surface becomes extrinsic influencing factor to alter self-assembly of BCP. At the same period, the study of the influence of 3D confinement to BCP nanoparticles generated by emulsion technique is also ongoing. Yang's group has demonstrated experimental studies of BCP nanoparticles generated by emulsion method.[34] They first studied curvature-induced deformed nanostructure at smaller ratio of the particle diameter to the feature spacing ($D/L_0 < 20$) by using cryo-ultramicrotome and transmission electron microscopy, which clearly revealed commensurability effect on the inner structure of BCP nanoparticles under strong spherical confinement. By blending symmetrical polystyrene-*b*-polybutadiene (PS-*b*-PB) and PS homopolymers in emulsion droplets, they observed unprecedented microphase in particles depending on commensurability. They further noticed the interface-driven morphological evolution of symmetric PS-*b*-PB.[35] To control the surface preferences of PS-*b*-PB at the emulsion interface, a mixture of two amphiphilic diblock copolymers, polystyrene-*b*-poly(ethylene oxide) (PS-*b*-PEO) and polybutadiene-*b*-poly(ethylene oxide) (PB-*b*-PEO), was used as surfactant. Obtained particle morphology, onion-like, prolates of stacked lamellae or terrace-like, is directly related to the mixed ratio of PS-*b*-PEO and PB-*b*-PEO. Particularly, non-spherical particles of diblock copolymers associated with the anisotropic interfacial energy were observed. These distinguished researches enrich our knowledge of novel structures of BCP nanoparticles through self-assembled process. In addition, membrane-extrusion emulsification approach has also been used in the fabrication and investigation of BCP nanoparticles.[36-40] Deng et al. have reported a series of successful fabrication of BCP nanoparticles with controllable surface pattern and internal structures. Wyman et al. have carefully summarized the self-assembled BCP nanoparticles generated by emulsion method in their review articles.[28]

Zhang et al. have reported their fabrication of diblock and triblock copolymer NPs by aerosol method.[41-43] Poly(3-(triethoxysilyl)propylmethacrylate)-*b*-polystyrene (PTEPM-*b*-PS)[42] and Poly(3-(triethoxysilyl)propyl methacrylate)-*b*-polystyrene-*b*-poly(2-vinylpyridine) (PTEPM-*b*-PS-*b*-P2VP)[41] onion-like particles can be changed to hybrid particles by cross-linking PTEPM blocks. Gold NPs are layered-arranged in these onion particles due to the affinity of $AuCl_4^-$ with pyridine groups.[43] Rahikkala et al. have also investigated the microphase nanostructure of polystyrene-*b*-poly(4-vinylpyridine) (PS-*b*-P4VP) NPs generated by aerosol method.[44] In their case, the self-assembly is induced by initial solvent evaporation and subsequent thermal annealing which is produced in gas phase. Their study shows that the assembly of BCP nanoparticles can be manipulated in the gas phase and annealing temperature is an additional tuning parameter. Nykänen et al. have fabricated thermosensitive submicrometer-sized polystyrene-*b*-poly(N-isopropylacrylamide)-*b*-polystyrene (PS-*b*-PNIPAM-*b*-PS) particles by using aerosol technique,[45] showing onion-like, gyroid-like and spherical morphologies having PNIPAM matrix and physically cross-linking PS domains. After swollen in water at 20 °C, which is lower than the PNIPAM coil-globule transition temperature, NPs become gyroid-like morphology.

Yabu et al. demonstrated their excellent research of generating BCP nanoparticles by using slow-precipitation process, which is named as self-organized precipitation (SORP) method.[46-52] Regular-sized poly(styrene-*b*-isoprene) (PS-*b*-PI) NPs were formed after evaporation of a good solvent from a polymer solution containing a non-volatile poor solvent and a volatile good solvent. The surface pattern of these symmetric BCP nanoparticles is stacked lamellae, Janus-like, tennis-ball-, mushroom-, wheel- and screw-like structures, depending on the diameter of the nanoparticle (Figure 2). This study typically demonstrated the effect of 3D confinement to the self-assembled morphology.[52] On the basis of this fabrication strategy, they further prepared polymer NPs with an inner structure of stacked lamellae phase separation which is composed of PS-*b*-PI and homo-polystyrene blends. After cross-linking one polymer moiety and dissolving the other, BCP nanodiscs, nanorings and nanowires were generated for the first time.[48,50] Blends NPs with more complex inner structures have been generated by mixing BCP with homopolymers[51] or two BCP (PS-*b*-PI/PS-*b*-P2VP and PS-*b*-PI/PI-*b*-P2VP).[53] On the other hand, they first observed the disorder-order phase transition and order-order phase transformation (stacked lamellae to onion-like) of phase separation structures in NPs induced by annealing in a poor solvent at different temperatures.[49] Furthermore, they explored 3D structural details of BCP nanoparticles by using TEM microtomography (TEMT).[54,55] Onion-like PS-*b*-PI NPs change to PI cylinders in a PS matrix upon chloroform annealing, and further divided into PS-core-PI-shell spherical structures in a PS matrix in extended annealing. The slight selectivity of chloroform for PS drives the transformation of nanoparticle's morphology.[54] Another new knowledge obtained from TEMT study is that complex structures are found only formed in the nanoparticle surface region, the thickness of which corresponded to the single-molecule length of the BCP in the bulk state.[55] In another word, the surface pattern and inner structure may be different in some cases. Surface pattern decides surface reactivity and wettability of BCP nanoparticles; in contrast, inner structure shows negligible effect on these properties, but it is significant in loading and releasing drugs by using BCP nanoparticles as nanocarriers. By using SORP method, other researchers also reported that water content and water temperature during the exchange of solvent and nonsolvent (water), also show influences to the surface pattern and inner structure of obtained fluorine-containing BCP nanoparticles.[56] Particularly, for poly(ethylene oxide)-*b*-poly(octadecyl methacrylate) (PEO_{39}-*b*-$PODMA_{17}$), in which PODMA block provides a temperature-responsive property, temperature will induce structural transition: at room temperature the internally bicontinuous aggregates formed at 4 °C undergo an order-disorder transition of the microphase separated domains which can be observed by using cryo-electron tomography.[57] The unique structural transition in PEO_{39}-*b*-$PODMA_{17}$ NPs system shows a possibility of temperature-controlled release. In addition, Yabu et al. also reported that the microphase separated structures in PS-*b*-PI NPs can be changed by microwave annealing in nonsolvent.[58] On the other hand, by replacing THF with chloroform and water with dodecane, Lim et al. found that the unperfected nanostructure of symmetric PS-*b*-P2VP NPs due to fast precipitation in THF/water system can be avoided, resulting in BCP nanoparticles with perfect onion-like morphology.[59] Moreover, Fan and Jin reported that onion-like PS-*b*-P2VP NPs can be generated by using asymmetric BCP.[60] Asymmetric PS-*b*-P2VP can form vesicle in acetone/water system, leading to the formation of onion-like BCP nanoparticle; however, spherical micelles are generated in THF/water system, and results in the NPs with large composed micellar structure. Moreover, they produced BCP nanoparticles with diameter of only 50-60 nanometers by directly freezing initial micelles, which may be more suitable to be used as nanocarrier for drugs.

Jin's group has also developed another strategy to fabricate BCP nanoparticles.[61] The obtained NPs have controllable size and orderly hexagonally-arranged-dot surface pattern. This dot pattern can be further transformed into a ring pattern on PS-*b*-P2VP NPs.[62] Both pattern can further be loaded with gold NPs through manipulation of swelling and complexing of $AuCl_4^-$ with 2VP and photoreduction *in situ*.[62] On the basis of this fabrication strategy, core-shelled and snowman-shaped PS/PMMA, PS-*b*-PB/PMMA composite particles can be produced easily.[63] A trace swelling solvent also can change the shape of BCP nanoparticles, from spherical to tablet-like, thus enriches the architectural diversity of BCP nanoparticles.[63] Patterned BCP nanoparticles can be further changed to mesoporous NPs by selectively swelling P2VP blocks.[64,65] The controllable formation of porous channels and individual pores in mesoporous PS-*b*-P2VP NPs provides good templates for synthesis of hybrid nanostructures, and the enlarged surface area of mesoporous nanostructures also enhances their loading capacity.

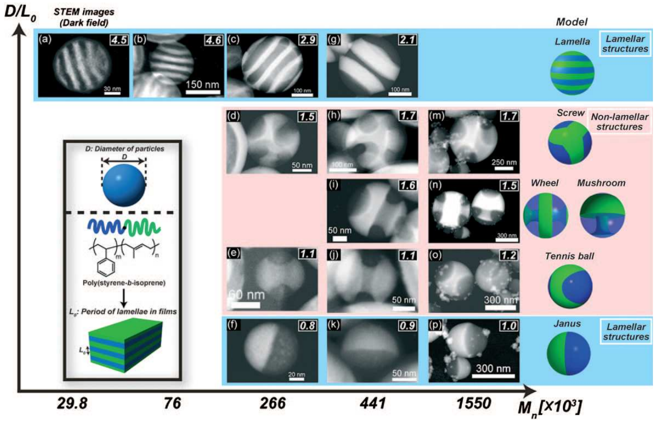

Fig. 2 Microphase separation structures in poly(styrene-*b*-isoprene) (PSt–PI) block copolymer nanoparticles as a function of molecular weight and the D/L_0 ratio, where D and L_0 correspond to the particle diameter and the period of lamellar structure in the films, respectively. STEM images of (a) a PSt–PI-30 nanoparticle, (b) PSt–PI-76 nanoparticles, (c–f) PSt–PI-266 nanoparticles, (g–k) PSt–PI-412 nanoparticles, and (m–p) PSt–PI-1550 nanoparticles. The D/L_0 ratios are shown in the upper-right corner of each STEM image. Reprinted with permission from ref. 52. Copyright 2008, John Wiley and Sons.

Other interactions, such as crystallization and hydrogen bond, are also used to tune nanostructures of BCP nanoparticles. Soininen et al. reported the formation of hierarchical structures of lamellae-forming BCP (PS-*b*-P4VP) within NPs by changing volume fraction of side chains, which are liquid-crystalline molecules (cholesteryl hemisuccinate, CHoIHS) and connected with BCP backbone (PS-*b*-P4VP) via hydrogen bond. NPs with complex internal structures, such as onion-like with single CHoIHS layers sandwiched between P4VP rich lamellae, or smectic P4VP(CHoIHS) layer perpendicular to the polymer domain interfaces are obtained through aerosol method.[66] Because of the reversibility of hydrogen bond, the CHoIHS side chains are able to be selectively removed from these BCP nanoparticles, leading to a kind of BCP nanoparticles with switchable internal nanostructures.

Theoretical study indicates that controlling the interfacial interaction will lead to dramatic change in shape and morphology of BCP particles. The property of surfactant is critical to the formation of microphase-separated nanostructure of BCP nanoparticles. Deng et al. observed that poly(vinyl alcohol) (PVA) as surfactant can modify the shape and microphase-separated morphology of PS-*b*-P4VP NPs.[38] Ku et al. have reported that the aspect ratio of CuPt nanorod surfactants have influence on the shape and internal morphology of BCP nanoparticles.[67] Similarly, the external shape and internal morphology of PS-*b*-P4VP particles are controlled by location of size-controlled Au surfactants NPs.[68] Au-based surfactant NPs adsorbed at the interface in PS-*b*-P2VP emulsion droplets generated by membrane-extrusion emulsification method afford asymmetric ellipsoid particles.[37] Klinger et al. observed that surfactant's property of cetyltrimethylammonium bromide (CTAB) and ω-hydroxyl CTAB (HO-CTAB) can tune the phase separation of symmetric PS-*b*-P2VP NPs.[69] Onion-like (PS is the outmost layer), reverse-onion (P2VP is the outmost layer) and prolate ellipsoid with axially stacked lamellae PS-*b*-P2VP NPs are generated depending on the mass fraction of mixed surfactants of CTAB and HO-CTAB. A further cross-linking of P2VP domains will result in a pH-triggered dynamic shape change for particles.

Moreover, the addition of small molecules which have strong interaction with one block in BCP not only impacts on microphase separated nanostructures of BCP nanoparticles, but also provides a general path to create hybrid BCP nanoparticles. Au NPs with PS ligands were located within PS-*b*-PB domains through changing lamellar domain spacing and the density of PS chains on the Au NPs.[70] Yabu et al. have fabricated hybrid BCP nanoparticles through directly mixing BCP with Au NPs by SORP.[71] The increase of Au NPs concentration shows influence to the inner morphology of obtained hybrid Au/BCP particles. Pyridine is an active functional group, therefore, pyridine in PS-*b*-PnVP (n = 2, 4) can work as structure-directing agent to generate mesostructured oxide particles, or as a ligand to fabricate BCP nanoparticles loaded metal particles.[72] The interactions of pyridine with other small molecules, such as forming complex with $AuCl_4^-$, forming hydrogen bond with pentadecyl phenol (PDP), electrostatic interaction with pyrenebutyric acid, are often used to modify the nanostructure of PS-*b*-PnVP (n = 2, or 4) NPs indirectly. For example, the addition of hydrophilic guest molecular PDP increases the volume fraction of PnVP block and alters the self-assembled nanostructures of hybrid PS-*b*-PnVP/PDP NPs.[40,73] Porous PS-*b*-P2VP NPs can be formed by selective removal of guest molecules.[40,73] Quantum dots are also incorporated into BCP nanoparticles with tunable- aggregated location.[74] Kim et al. observed that the addition of CTAB into $AuCl_4^-$@PS-*b*-P4VP microspheres will selectively extract Au precursors located near the surface of microspheres because of the strong electrostatic attraction between the CTAB and Au precursors, resulting in regular-patterned porous nanostructures on the surface of hybrid microspheres.[75] Because the acidic nature of Au precursor, P4VP domains can be selectively swollen, resulting in gold-decorated PS-*b*-P4VP NPs with various surface nanostructures.[76] Phosphotungstic acid and pyrenebutyric acid have affinity to P2VP domains, resulting in hybrid NPs which follows the original microphase separated nanostructures of PS-*b*-P2VP in precipitation process.[60] However, pyrene doesn't have strong selectivity to any blocks in PS-*b*-P2VP and it shows evenly-dispersed in BCP nanoparticles, without clear segregation in two domains.[60] Moreover, by adding hexadecane as liquid core in PS-*b*-PMMA copolymer NPs prepared by miniemulsion process, double nanoconfinement in colloids, which is the NPs diameter D and the shell thickness d, was studied for the first time.[77] The study of the dispersion and location of guest molecules is very important in preparing drug-delivering system based on BCP nanoparticles. The different location of guest molecules will result in difference in releasing, which is a key factor to evaluate drug-delivering system. Particularly, popular drug-delivering polymer particles are hydrophilic in nature, which is immiscible with some strong hydrophobic drugs, such as curcumin, DOX and so on. If these traditional delivering cargos are replaced by BCP nanoparticles which have both hydrophilic and hydrophobic domains, that may advance the loading of hydrophobic drugs. Furthermore, two drugs with different properties, one hydrophilic and one hydrophobic, may also be loaded and located in BCP nanoparticles separately. Their release can be triggered by different stimulants and the process will be asynchronous, which may be good for multidrug-delivering system. On the other hand, the developing of target-delivering and visible-delivering requires multiple functions of delivering cargos: loading drugs, modifying with target molecules, containing fluorescent or photo-thermal functional NPs. These loading molecules and NPs have different property and chemical reactivity, thus simply mixing them in delivering particles may lead to interference with each other, for example, fluorescent particles and molecules may be quenched by other molecules and lose their effectiveness.

In all NPs with different nanostructures, Janus particle is most attractive and unique because of their wide potential applications as emulsifier and electroresponsive photonics.[78-82] Janus particle has symmetric shapes and patterns, and its two sides have distinct chemistry and wettability.[83,84] Walther and Müller have summarized different architectures of Janus particles, ranging from simple spherical to dumbbell shapes, vesicles/capsules, cylinders and disks.[83] Yang's group has reported a series of works on Janus particles and Janus composites.[39,85-87] Christian et al. fabricated Janus vesicles by using calcium ions to complex poly(acrylic acid) (PAA) in PB-*b*-PEO/PB-*b*-PAA, getting completely phase-separated Janus vesicles.[88] Janus micelles can be generated by combining AB and BC diblock copolymers in which B is insoluble and as a micellar core;[89] or mixing AB and CD diblock copolymers in which B and C are miscible and connected together as core part, leaving A and D separately outside; or from ABC triblock terpolymers.[34-37,90,91] Janus discs containing an inner cross-linked polybutadiene layer and two different outer sides of polystyrene and poly(tert-butyl methacrylate) are generated via a template-assisted synthetic pathway followed by sonication.[92] Moreover, Janus polymer particles can be generated by using the phase separation of two homopolymers.[63] Deng et al. reported a kind of NPs with more complex inner structures, in which one half is PMMA, the other half is PS-*b*-P4VP with tunable nanostructures generated by phase separation.[39] Stimuli-responsive (pH) Janus particles in current studies show switchable surfactant properties in response to solution pH.[93,94] Recently, Lu and Urban reported a synthesis of Janus balance-tunable NPs utilizing a two-step emulsion polymerization of pentafluorostyrene and 2-(dimethylamino) ethyl methacrylate and n-butyl acrylate (nBA) in the presence of poly(methyl methacrylate)/nBA NPs seeds.[94] These Janus NPs are able to stabilize oil droplets in water at high pH by Pickering emulsions, which at lower pH release oil. These studies open up a new application field for BCP nanoparticles with unique structural feature.

4. Conclusions and outlook

BCP nanoparticles with compartmentalized internal structures can be generated by tuning BCP composition, commensurability (size), interfacial interactions between two blocks and surrounding environment by various surfactants, additional small molecules and surface properties of hard templates. Recent studies not only focus on the manipulation of nanostructures and shape of BCP nanoparticles, but also utilizing these nanostructures to create multifunctional devices and carriers. Robb et al. fabricated well-defined BCP containing an alkyne-functional, biodegradable polylactide (PLA) block and conjugated it with azide-functional coumarin dyes *via* click chemistry.[95] The release of covalently connected molecules was controlled *via* the degradation of PLA scaffold under physiological conditions. Self-assembled NPs show their potential as next generation of delivery vehicles with multiple functionalities and compartmentalized internal structures. Another interesting application of nanostructured BCP nanoparticles is demonstrated by Ku et al.[68] Convex lens-shaped BCP nanoparticles were produced by using size-controlled Au NPs as surfactants. These BCP nanoparticles can be further changed to porous nanostructures with vertically ordered channels within the particles, which can be used as a microlens, leading the light to concentrate toward the focal point with enhanced near-field signals. If well-ordered Au cylinders are filled into channels, these particles will show unique distribution of light scattering. Furthermore, they also demonstrated the fabrication of multicolour emitting microspheres with 3D controlled nanostructures.[74] Spatial separation of different-colored quantum dots (QDs) *via* supramolecular assembly controls the Förster resonance energy transfer efficiency between QDs. Their exploration opens up a broad and new application field for BCP nanoparticles in optical, biological-sensing and imaging applications. In addition, Janus BCP nanoparticles show promising applications in emulsion and oil-removal.[94] Mesoporous BCP nanoparticles generated by selective swelling[64] or removing some compositions[40] are also promising candidate for template-fabrication or loading-matrix with enlarged surface area. On the other hand, to meet the requirement of nanomedicine, the combination of shape- and nanostructure-controlling is urgently needed. More and more investigations reveal that many physiological reactions have responsibility to the geometry of targets.[96-98] Shape-specific NPs show unique biological and pharmacological properties, leading to the development of shape-specific polymeric nanomedicine.[99] Shape-changing of BCP nanoparticles is often observed accompanied with the transformation of internal morphology of BCP nanoparticles. Recently, Hawker's group reported a facile methodology to ellipsoidal BCP nanoparticles, which have stacked lamellae nanostructure, shape anisotropy, and pH-triggered anisotropic swelling profile.[69] It is the first report to incorporate three main structural features into a single nanoparticle system: shape-anisotropy, internally structured morphology and stimuli-responsiveness. It demonstrates the new development of BCP nanoparticle-based drug delivery system.

However, because polymerization of BCP requires highly controlled non-aqueous experimental conditions, such as anionic polymerization, fabrication of BCP nanoparticles directly by using emulsion method cannot be applied to different kinds of BCP. For commercial application of nanostructured BCP nanoparticles, the most important breakthrough is synthesis of BCP nanoparticles with self-assembled nanostructures by one-pot. Recently, new synthesis strategies have been reported, showing that great advance in this field is emerging. Jennings et al. reported a one-pot synthesis for well-organized BCP microparticles, which is easily adapted to commercial scale.[100,101] Their synthesis method combines reversible addition-fragmentation chain transfer (RAFT) polymerization with dispersion polymerization in supercritical carbon dioxide. A wide range of monomer types, can be applied in this polymerization process, generating microparticles with nanoscale ordered morphology. Moreover, they found that the chemical nature of polymer blocks influences their selective CO_2 sorption and further results in a modification of BCP phase behaviour. Zhang et al. also reported their successful fabrication of concentric vesicle particles *via* RAFT dispersion polymerization.[102] NPs of ABC triblock copolymers with temperature-sensitive nanoparticle-to-vesicle transition are synthesized by seeded dispersion RAFT polymerization.[103] Now rapid synthesis of ordered quasi-multiblock copolymers (including BAB, CBABC, ABC and ABCD) can be achieved in automated synthesizer by utilizing RAFT polymerization protocols.[104,105] RAFT dispersion polymerization method recently presents great advances for generation of BCP aggregates.[106] The further development of polymerization strategy will greatly advance experimental investigations and commercial applications of nanostructured BCP particles.

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Notes and references

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