Feature article

Encapsulation of inorganic nanoparticles into block copolymer micellar aggregates: Strategies and precise localization of nanoparticles

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ABSTRACT

Precise assembly and localization of preformed inorganic nanoparticles (NPs) in block copolymer (BCP) assemblies are of great importance in realizing the formation of nano-hybrids with high performance. Properties of the nanocomposites depend not only on those of individual building blocks but also on their spatial organization at different length scales, demonstrating unique optical, electrical, and magnetic properties. With the aid of the BCPs, NPs can form a broader range of structures in the nano-scopically confined geometry. Thus, many studies have focused on the selective localization of NPs in BCP aggregates. In this paper, we will outline recent advances in the preparation strategies for precise localization of inorganic NPs into BCP micelles, including co-precipitation, supramolecular assembly, interfacial instabilities of emulsion droplets, heating–cooling, electrostatic interaction, and others. Manipulating the balance between enthalpic and entropic contributions provides one of the opportunities to precisely control the spatial distribution of NPs in BCPs assemblies. We will focus on the principles of precise control of dispersion and localization of the NPs in BCP micelles. Potential applications of the hybrid micelles will finally be discussed, followed by the summary and outlook of this emerging area.

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1. Introduction

Nanoparticles (NPs) exhibit unique properties associated with optical, electrical, and magnetic behavior, which are different from the properties in their bulk materials [1]. Ensembles of NPs may exhibit properties different from those of the individual building blocks due to coupling and exchange phenomena. Collective properties of nanostructured arrays of NPs can be accessed by tailoring the spatial arrangement of the NPs over multiple length scales [2]. Recent development in NPs synthesis provides a plethora of inorganic NPs, building the foundation for constructing hybrid nanocomposites with unlimited possibilities.

Amphiphilic block copolymers (BCPs) can self-assemble into various nanostructures such as spherical/cylindrical micelles, lamella phases, or vesicle membranes depending on block ratio of the BCPs, solubility of the blocks in the solvents, solvent composition/concentration, immiscibility of the solvents, and temperature/pH of the solutions [3–8]. These predictable BCP aggregates have attracted considerable interest not only for academic reasons, but also because of potential applications in the fields of medicine, biology, electronics, and catalysis. Particularly, the self-assembled nanostructures can be utilized as nanotemplates to synthesize semiconductor or metal NPs with controlled size and morphology or to direct metal NPs deposition and further control the spatial distributions of NPs at one to three dimensions [9–16].

Recently, many studies have focused on the encapsulation of NPs into BCP aggregates since these hybrid aggregates can combine the properties from the parent constituents and generate new properties to meet the requirements in applications such as labeled materials, photonic nanodevices, or chemical sensors [17]. Encapsulation of NPs in BCP micellar aggregates can serve many purposes: (1) Improving stability: The stability of NP suspension is often critically dependent on the structure of ligands that are bound to NP surface. Several methods have been developed to...
stabilize NPs and to maintain their properties in water, including surface functionalization by small molecules, polymers, or biomolecule ligands [18]. However, over long period of time, these ligands can dissociate. Even a strong thiol ligand could dissociate from Au surface under the environment of high temperature, competing biological thiols, and chemical cleaving agents, not to mention ligands bond by weak interactions [19–22]. Encapsulation of NPs in the BCP micelles provides a suitable environment for further stabilizing the NPs. After cross-linking, the hybrid micelles will be substantially more stable to heat and pH, allowing them to be more useful in biological or biotechnological protocols requiring harsh conditions [23]. (2) Reducing toxicity [24]: As-synthesized NPs are normally coated with bilayer of surfactant molecules, for example, cetyl trimethylammonium bromide (CTAB), on gold NPs. Yet, clinical applications of these photothermally active NPs are currently limited by the cytotoxicity of CTAB, and also the nonspecific uptake of CTAB-coated NPs [25]. Several approaches have been developed to replace the original CTAB coating with a new enclosure formed by other materials, including the commonly-used conjugation of NPs with poly(ethylene oxide) (PEO) thiols. Yet again, this method does not normally produce dense PEO brushes, and incomplete coverage of gold NPs with PEO has been shown to result in insufficient stability of the NPs against aggregation and under physiological conditions [26]. Encapsulation of NPs in the core of the micelles can reduce the potential toxicity of NPs. (3) Easy to be multi-functionalized: An alternative approach used to fabricate multifunctional NPs is to simultaneously incorporate different NPs within a nanoscale micellar carrier [27]. In this case, each component can be prepared in monodisperse form prior to encapsulation, and size/composition of the products can be closely controlled, the general self-assembly method can provide multiple-core NPs with predictable physical properties. (4) Improving collective properties: Controlled clustering of magnetic NPs inside BCP aggregates results in high particle loading and a considerable increase in detection sensitivity in magnetic resonance imaging (MRI) [28–30]. Moreover, the aggregates loaded with magnetic NPs and drugs can be directed on the targeting locations by magnetic fields [29]. Drug release can be controlled through an oscillating magnetic field producing local hyperthermia in the magnetic particle loaded portion of the aggregates, which requires the precise localization of NPs in the corresponding parts of the aggregates (e.g., micelle core or vesicle walls) [28]. (5) Serving as template for functional cavity formation: The encapsulated NPs can serve as a sacrificial nanotemplate for hollow polymer capsules formation by cross-linking of the resultant polymer shell, followed by removal of the template of NPs [31–33].

When NPs have been encapsulated into the BCP micellar aggregates, many factors, including the content, distribution, orientation, and localization of NPs in the polymer matrix should be considered, which play significant roles in determining the properties and performances of the polymer nanocomposites. Each micelle contains three different kinds of regions, including core, interface, and corona, among which NPs can be localized selectively in different regions by using the suitable methods [34]. Precise control of NPs location within BCP aggregates demonstrates many advantages [11]: (1) Locating NPs in the micellar core: Encapsulation of quantum dots (QDs) in the core of the polymer micelles can not only improve the stability of the NP and reduce toxicity to animal body, but also could preserve the unique optical performance of QDs [24]. Incorporation of NPs in the center of micelles might be useful in the area of labeling or catalytic applications, where the particles need to be protected on all sides by the hydrophobic wall-forming materials. For example, a thin polymer layer (∼10 nm), which is easily penetrated by small organic molecules, but with much more difficulty by inorganic ions, acting as a barrier to inorganic ions, which might poison the catalyst, at only a slight cost in overall speed of the reaction. In addition, the central localization can provide equal protection for all the NPs, rather than having some more exposed to the potentially toxic environment than others if the NPs are randomly located within the wall [35]. (2) Locating NPs in the core and corona: Separated electron—donor and electron—acceptor in different domains with tailored spacing will be beneficial for the optoelectronic applications. The micellar scaffold that contains specific domains can be used to partition different species in micelles. For example, when QDs were located in the corona and conducting polymer (e.g., poly(3-hexylthiophene) (P3HT)) was encapsulated into the core of the micelles, the excited-state photoluminescence quenching of the QDs occurred in this case, induced by the P3HT, enabling electronic energy transfer between the QDs and the P3HT [36]. On the other hand, when fluorophores or QDs are in close proximity to metal NPs, QD—metal interaction can result in either enhancement or quenching of photoluminescence (PL) emission. Very short distance (<5 nm) between QDs and metal NPs gives rise to PL quenching [37], whereas longer separation (∼10–20 nm) leads to distance-dependent PL enhancement [38]. BCP assemblies offer precise location control of embedded NPs, necessary for varying their optical properties by tuning the exciton—plasmon coupling ratio between QDs and metallic NPs. Recently, Farinha et al. [39] encapsulated QDs in the core of the micelles and incorporated Au NPs in the coronas with a precise distance between QDs and Au NP of ∼20 nm. The precise spacing between QDs and Au NPs prevents any quenching of QDs PL by the metal NP and leads to an apparent enhancement of QD PL emission (∼8 times) relative to QD emission from micelles without Au NPs [39].

Until now, there are two main methods to incorporate NPs into BCP micelles, one is in situ method (NPs can be formed in situ inside the BCP micelles by using chemical reaction [9]), while the other is ex situ method (co-assembly of the preformed NPs and BCPS [40]). By comparison, the latter approach offers an effective means to precisely control size and position of NPs in BCP micelles. In this feature article, we will first discuss the preparation strategies for precise localization of preformed inorganic NPs into BCP micelles. Then, we will review various factors affecting precise localization of the NPs in the micelles and the possible mechanisms of this area. Finally, we will end with possible applications of the hybrid micelles in biomedical area, catalysis, sensors, etc., followed by a brief outlook on the future trends in this emerging area. Considering the topic, studies on encapsulation of preformed NPs into polymer bulk or thin films and the in situ methods are not included in this paper, detailed reviews covering the above aspects have been published elsewhere [41–46].

2. Strategies for encapsulation of preformed NPs into BCP micelles

2.1. Co-precipitation method

Encapsulation of preformed inorganic NPs into BCP micelles can be performed through co-precipitation method—co-assembly of NPs and amphiphilic BCPS in selective solvent. In 2005, by using the co-precipitation approach, Taton group prepared hybrid micelles based on amphiphilic BCPS poly(ethylene glycol)poly(acrylic acid) (PS—PAA) and gold NPs (Fig. 1) [47]. Typically, homogeneous solution was first prepared by dissolving PS—PAA and citrate-capped Au NPs in a good solvent such as N,N-dimethyl-formamide (DMF). Selective solvent (e.g., water) simultaneously desolvated the NPs and the hydrophobic polymer block (PS), leading to the aggregation of the NPs with the hydrophobic block, forming hydrophobic parts of the
aggregates (e.g., micelles cores), which were protected by the hydrophilic segment (PAA). Hydrophilic PAA shell can stabilize the hybrid micelles and remains soluble in water, which also can be crosslinked by using crosslinker such as N-ethyl-N′-(3-dimethylaminopropyl) carbodiimide (EDC) that effectively avoids dissociation in organic solvent. During the micelle formation process, to induce the Au NPs into hydrophobic core, dodecanethiol is usually used to modify and renders the Au NPs hydrophobic. This process sacrifices the entropy term but prevents a larger enthalpy penalty from energetically unfavorable hydrophobe–water interactions and therefore lowers the free energy of the system. It has also been demonstrated that this approach can be easily used with combinations of NPs to construct multifunctional particles possessing several desirable properties in a single hybrid micelle with various morphologies. For the NPs positioning in this method, NPs can be dispersed uniformly in BCP micellar aggregates or localized in the center of hybrid micelles.

On the other hand, Park et al. dissolved PS$_{193}$–PAA$_{41}$ together with trioctylphosphine oxide (TOPO)-stabilized CdSe/ZnS core–shell QDs in mixed common solution of DMF and chloroform. Water was

![Fig. 1](image1.png)

**Fig. 1.** (a) Schematic illustration of preparation of hybrid micelles based on PS–PAA and Au NPs. (b, c) TEM images of micelles filled with Au NPs of diameter 4.1 ± 0.5 nm and 12.3 ± 1.1 nm, respectively. (d) TEM image of wormlike micelles prepared from nanostructures with different shell thicknesses. Reprinted with permission from Refs. [47,111,147].

![Fig. 2](image2.png)

**Fig. 2.** (a) Schematic description of the formation process and cross-sectional structure of the hybrid BCP micelles. (b) Three-dimensional representation of the hybrid micelles. Green dots represent the QDs assembled at the spherical interface between the polymer core and the shell. (c) Experimental and calculated radial intensity profiles of TEM images of hybrid micelles. Right: The TEM image used in the analysis. The colored arrows indicate the corresponding positions. Reprinted with permission from Ref. [49].
slowly added to the above mixture to induce the co-assembly of the BCPs and QDs. The resulting assemblies could be obtained after dialysis and purifying treatments. Differing from the above mentioned co-precipitation method [47,48], one of the advantages of this method is that it can allow for the radial distributions of NPs in the BCP micelles by simply changing the molar ratio of copolymers to NPs (Fig. 2) [49]. The QDs incorporated in the polymer assemblies can maintain the high quantum yield similar to that of the original NPs in chloroform and are very stable in aqueous solution over a period of months.

Instead of adding selective solvent to polymer solution, Gao and co-workers slowly added tetrahydrofuran (THF) solution containing poly(3-caprolactone)–poly(ethylene glycol) (PCL–PEG) and hydrophobic magnetic NPs to a large amount of water under sonication and stirred to evaporate the THF. The hybrid micelles with encapsulated NPs were generated during the THF evaporation and separated by magnetic field-guided accumulation. During this process, drug can also be encapsulated into the core of the micelles [28,50].

2.2. Interfacial instabilities of emulsion droplets

Encapsulation of NPs into the micelles can also be performed through interfacial-assisted assembly at the emulsion droplets. Instead of dissolving PS–PEO and hydrophobic NPs in water miscible solvent (e.g., THF), Zhu and Hayward used a water-immiscible organic solvent (chloroform) which was a good solvent for both blocks of the BCPs [51,52]. The polymer solution was next dispersed as emulsion in a continuous aqueous phase with poly(vinyl alcohol) (PVA) as the stabilizer, followed by removal of solvent from the droplets by diffusion through the aqueous phase and evaporation. As the concentration of BCP within the droplets increased, self-assembly of the polymer took place through a series of interfacial instabilities, where the droplets spontaneously increased in surface area and ultimately ejected micellar assemblies into the aqueous phase. During the hydrodynamic processing, hydrophobic NPs can be effectively encapsulated into the core of the micelles, as shown in Fig. 3 [51]. Micropipette aspiration measurements performed on evaporating chloroform droplets containing PS–PEO revealed that interfacial instabilities were correlated to an approach of the organic/water interfacial tension to zero [53,54]. Addition of sodium dodecyl sulfate (SDS) to the aqueous phase lowered the interfacial tension, thereby facilitating the onset of instability at low concentrations of PS–PEO within the droplets. Furthermore, increased amounts of SDS led to qualitatively different mechanisms of interfacial instabilities and corresponding different morphologies of the resulting assemblies.

One of the advantages of this approach is the ability to produce either spherical or worm-like hybrid micelles. The micellar morphology depends sensitively on the composition of the copolymer and this method can be applied to a range of copolymers with different hydrophobic blocks [52]. Moreover, this method can be applied to produce multifunctional micelles by simply encapsulating iron oxide NPs and QDs or two kinds of QDs for simultaneously realizing magnetic manipulation and fluorescent imaging, respectively [55–57]. For the case of cylindrical micelles, loading is found to be both efficient and rather uniform, with essentially every micelle containing encapsulated NPs. For spherical micelles, the uniformity of NPs loading is not as high, but simple centrifugation or magnetic separation steps could allow for straightforward
enrichment of samples to ~90% of loaded micelles. The encapsulation behavior of hydrophobic NPs is found to be insensitive to particle surface chemistry (TOPO, dodecanethiol, and oleic acid/oleylamine), shape (spherical and rod-like), and size (from ~1 to 20 nm), thus providing a flexible route to fabricate multifunctional spherical and cylindrical micelles. Due to their combined features, these hybrid micelles have great potential in cell biology, biophysics, and fluid mechanics.

2.3. Heating–cooling method

In co-precipitant approach, asymmetric copolymers with longer hydrophobic block can usually be used, which give rise to crew-cut micellar shell, where polymers with longer hydrophilic chains fail to do so [18,47]. Chen’s group demonstrated a heating–cooling route to generate hybrid micelles by employing longer hydrophilic chains and short hydrophobic segment to form hairy micelles, as shown in Fig. 4 [40]. The use of such copolymers for NP encapsulation requires conditions differing from the co-precipitant approach. Briefly, a BCP (e.g., PS−PAA or PS−poly(glutamic acid), (PS−PGA)) solution containing hydrophobically functionalized Au NPs is first heated to 110 °C for 2 h, and then slowly cooled down, finally forming hybrid micelles due to the self-assembly of the copolymer.

By comparison with the co-precipitant route [47,48], there are at least two advantages in this approach. One is that BCPs with longer hydrophilic chains can be used to prepare hybrid micelles, which not only can stabilize the micelles in solution without chemical crosslinking but also can allow encapsulation of single small Au NPs. The other is to avoid mixing of two solution phases which could introduce regional inhomogeneity and aggregation. Small Au NPs (diameter < 10 nm) can be singly incorporated into polymer micelles and the production ratio of core/shell micelles is above 98%. Moreover, this method can lead to thick hydrophilic shell which can make biomolecules to securely attach. Two or three NPs can also be encapsulated into one BCP micelle, forming dimer, or trimer clusters. Au NP dimers or trimers can be isolated by centrifuging a high density of CsCl solution and more than 85% of dimers can be obtained [58]. Furthermore, two kinds of Au NPs with different surface properties (A and B) can also be encapsulated into one BCP micelle, forming specific products of AB, AB₂, AB₃ and AB₄ [59].

2.4. Supramolecular assembly/disassembly route

Supramolecules can be readily constructed by attaching small molecules to polymer backbones via secondary interactions such as hydrogen bonding and ionic interactions. The phase behavior of BCP-based supramolecules in bulk and films has been extensively studied by ten Brinke and Ikkala, which provides useful information to guide initial studies in co-assemblies of NPs and BCP-based supra-molecules. The most extensively studied supramolecular system contains PS−poly(4-vinylpyridine) (P4VP) with 3-pentadecylphenol (PDP) small molecules attached to the 4VP groups through hydrogen bonding. The concept allows a rich variety of morphologies and phase transitions by modifying the block lengths, the amount of the amphiphiles, their alkyl chain lengths, and strength of the hydrogen bonding.
The combination of polymers and small molecules allows one to gain better control over the spatial organization of spherical and anisotropic NPs over multiple length scale [60]. Zhu and co-workers introduced a new concept to encapsulate NPs into the core of micelles based on the directed supramolecular assembly/disassembly [11] (Fig. 5). Typically, PS–P4VP and PDP are first dissolved in chloroform to form PS–P4VP(PDP)_x (x represents the molar ratio of PDP to 4VP units) comb-like supramolecules, which can further self-assemble into hierarchical structures. When PS-coated gold NPs are introduced into the supramolecule system, NPs are selectively incorporated in PS phase within P4VP(PDP) matrices after slow evaporation of the organic solvent. Due to the reversible nature of the hydrogen-bonding, isolated hybrid micelles can be obtained by disassembling the supramolecular system, e.g., rupturing the hydrogen bonding and removal of the PDP. For instance, by using PS_{20k}–P4VP_{17k} (volume fraction of PS: 56%) and PDP system, cylindrical micelles with uniformly dispersed gold NPs along the center-line can be realized by using this method.

Compared to the co-precipitation processing, this method provides a facile and robust way to prepare NP-loaded cylindrical micelles, which show more advantages such as high loading capacity of hydrophobic species per micelle. More importantly, NPs can be precisely localized into specific position of BCP micelles, which will enhance the properties of hybrid micelles significantly. The interparticle spacing and micellar morphology can be readily tailored by simply changing the synthesis conditions such as the NP or PDP content. This facile technique can be extended to other supramolecule pairs and NPs of different types although further work is required to fully understand the mechanism driving NPs to micelle core or broad distribution, and to fully define the roles of graft density, ligands and NP shape on the encapsulation. It is worth noting that, in the absence of PDP, NPs can also be incorporated into PS cylindrical domain of PS–PVP assemblies when volume fraction of PS is set in the range of ~0.16–0.32 [61,62]. However, it turns out that it is rather difficult to separate the PS cylinders using PVP-selective solvents probably because rather long PVP chains are required to obtain self-organized cylinder with a PS core. In order to disassemble the microstructures and obtain isolated nano-objects, external force, such as ultrasonication or vigorously stirring, has to be used which will usually disrupt the microstructures and induce some irregular structures.

In this approach, equilibrium state of the BCP/NPs in film or bulk state can be easily reached and morphology of the nanocomposites can thus be easily predicted. Several strategies can be employed to tune the morphology of the composites, distribution and orientation of NPs, including external forces (magnetic, electric, or shearing), and thermal or solvent annealing. For example, the oscillatory shear orientation of hierarchically ordered PS–P4VP(PDP)_x of a cylinder-within-lamellar morphology result in parallel alignment of the PS cylinder with the plane parallel to the shear plane and transverse alignment of the matrix layers. This result suggests that PS–P4VP cylinders of up to ~10 µm length can easily be prepared using the shear flow procedure [63,64].

2.5. Electrostatic interactions

Above-mentioned methods allow the localization of the NPs in micellar core or at the interface. Electrostatic interaction approach can realize the relatively precise localization of NPs in charged corona of the micelles. Firstly, BCPs with one charged block self-assemble into various micelles with different packing geometries through the precipitation method. Then, the oppositely charged NPs can further be adsorbed in the charged microdomain of micelles, forming hybrid micelles with NPs in the corona (Fig. 6a–c) [65]. For example, PAA–poly(methyl acrylate)–PS (PAA–PMA–PS) triblock copolymer has been chosen to form various micelles such as disks, toroids, one-dimensional cylindrical nanostructures in mixed solvent of THF/water and organic diamines. Au NPs were
modified with positive charges for realizing the electrical interactions with PAA block, which could be effectively adsorbed in the hydrophilic part with negative charges by electrostatic interactions, forming hybrid micelles.

On the other hand, selective patterning of the poly(ferrocenyldimethylsilane) (PFS) block co-micelles with Au NPs and PbS QDs via electrostatic interaction has been demonstrated by Winnik group (Fig. 6d) [66,67]. Typically, PFS–P2VP was used to create cylindrical micelles in 2-propanol with PFS as cores and P2VP as coronas. Quaternation of the P2VP coronas with Mel rendered the cylinders with positive charges. Afterward, PFS–P2VP assembled into the two ends of the positively charged micelles driven by epitaxial crystallization of PFS blocks, leading to the generation of triblock co-micelles with positively charged central block and non-charged end blocks. Subsequently, negatively charged Au NPs, or PbS QDs were added to the triblock co-micelle solution, allowing the negatively charged NPs to selectively bind to the positively charged central blocks of the co-micelles by the electrostatic interactions. In addition to use of amphiphilic BCPs with one charged block, double hydrophilic BCPs with one charged block have also been used for selective localization of charged NPs in the micelles through electrostatic interactions [68–71].

One of the advantages of this approach is that segmented nanostructure with spatially selective deposition of metal NPs can be realized by simply using co-micelles. The ability to control the deposition of NPs on PFS–P2VP cylindrical micelles provides a general route to realize functional hybrid nanomaterials that combine high shape anisotropy, polymer-mediated redox and mechanical behavior, conductive, magnetic, and photocatalytic properties.

2.6. Assembly of amphiphilic NPs

Inspired by the assembly of amphiphilic molecules, amphiphilic NPs can also be used as building blocks for realizing the fabrication of hybrid micelles or vesicles. To do this, amphiphilic NPs should be obtained firstly by tethering NPs with amphiphilic linear BCPs, V-shaped copolymers [72,73] or polymer mixture of hydrophobic and hydrophilic segments. These amphiphilic NPs can self-assemble into micellar-like aggregates, vesicles, sheets, and tubes [74,75]. For instance, Zubarev et al. synthesized PS–PEO diblocks containing a carboxylic group at the junction point and attached them to phenol-functional gold or silver NPs. Self-assembly of the copolymer-coated NPs in solution generated cylindrical micelles with NPs located at the interface between PS core and the PEO corona [72]. Meanwhile, when two homopolymers such as hydrophilic PEO and hydrophobic poly(2-nitrobenzyl acrylate) (PNBA) were to modify the gold NPs, the amphiphilic NPs can self-assemble into hybrid vesicles, which can be used to load anticancer drugs (e.g., doxorubicin) in the core for realizing the controlled-release application [74,76,77].

Generally, for NPs modified by mixed homopolymer brushes, the different bonding strengths and absorption kinetics of different polymers onto NPs make it difficult to quantitatively control or predict the relative density of each type of the polymer. BCP tethers offer greater control over the chemical functionality and composition (i.e., relative volume of hydrophilic/hydrophobic species) as well as architectural complexity of polymer chains on NP surface. To increase the structure tunability and precise control of the interparticle distance, amphiphilic BCPs have been used to modify the NPs. Föster and coworkers reported that amphiphilic QDs were prepared and self-assembled into vesicles directly. They coated

![Fig. 6.](image-url)
CdSe/CdS QDs with PEO-branched polyethyleneimine (PEO–PEI) through ligand exchange approach. Self-assembly of such NPs with low grafting density in solution produced vesicles consisting of a monolayer of the QDs in the walls [78], Nie et al. used PS–PEO–SH to modify Au NPs, which can assemble into various superstructures in a mixture of water/THF, including unimolecular micelles, clusters with controlled number of Au NPs, vesicles, and tubular assemblies [79,80].

Self-assembly of such amphiphiles predominantly depends on the hydrophobic/hydrophilic balance, i.e., the relative size of hydrophobic/hydrophilic components. For example, when BCPs with a long hydrophobic block or NPs with large diameters were used, the amphiphilic NPs self-assembled into vesicles, while tubular assemblies were generated for amphiphilic NPs comprising BCPs with a shorter hydrophobic block and NPs with smaller sizes. Also, interparticle spacing can be tuned by varying the molecular weight of the grafted polymers. This approach offers precise control over the interparticle distances, thus fine-tuning the plasmonic properties of assembled Au NPs [79,81]. The general strategy can be extended to assemble NPs with different dimensions and geometries (i.e., nanorods (NRs) and nanocubes) [73,75]. Moreover, these Au assemblies can be used as drug carriers and well dispersed in water, facilitating their biomedical applications in bioimaging and photothermal therapy of cancer based on the strong absorption in near-infrared range due to the remarkable plasmonic coupling of Au NPs [74,81].

Besides the above mentioned approaches for the encapsulation of NPs into the micelles, there are several other strategies, including film rehydration, nanoflash precipitation, microfluidics processing, hydrogen bonding of the NPs with the host BCPs, electrospun [82], layer-by-layer assembly of charged blocks on gold NPs surfaces [83], and miniemulsion polymerization and thiol-ene functionalization [84]. For the film rehydration method, a kind of phospholipid BCP such as n-PEG–phosphatidylethanolamine (PEG–PE) has been chosen to incorporate NPs (e.g., QDs) into the core of micelle [24]. One of advantages of this method is to use QDs without any surface modification during formation process. Otherwise, the hybrid micelles obtained are very regular in size, shape, and structure, which can further be used for in vivo imaging due to their PEG shell as excellent repellent for biomolecules. In addition, nanoflash precipitation method has been developed, which can incorporate hydrophobic organic compounds and inorganic NPs such as Au NPs into BCP micelles quantitatively [85,86]. For the formation process, inorganic NPs, hydrophobic drugs, and amphiphilic BCPs were first dissolved in a water-miscible organic solvent such as THF, dimethyl sulfoxide (DMSO), or ethanol. Then, the organic solvent stream and water intensely were mixed in a multi-inlet vortex mixer, which induced supersaturation and initiated rapid precipitation of all hydrophobic components, including the hydrophobic block of the BCP, finally forming the hybrid micelles. This method can effectively avoid disadvantages of conventional emulsification and solvent evaporation processes which would lead to low loading capacity and uneven distribution of hydrophobic components within NP interiors. On the other hand, the formed hybrid micelles have narrow particle size distributions, specified compositions, and long-term stability. This technique allows for the fabrication of multifunctional nanohybrids containing a variety of hydrophobic active compounds, fluorescent dyes, and inorganic NPs.

Rotello and coworkers reported the “bricks and mortar” strategy to encapsulate NPs into the micelles [87]. In one of their studies, a diblock copolymer with the first block of PS and a second block of a random copolymer of PS and dianinothiophene-functionalized styrene was prepared as the “mortar”. Thymine-functionalized Au NPs were employed as the “bricks”. Aggregation of the mortar and the bricks in solution produced micellar aggregates with multiple Au NPs in the cores through hydrogen bonding between the dianinothiophene groups in the copolymer and the thymine groups on the particles. The average size of the cores of the micelles can be controlled by adjusting the block length of the copolymer.

Liu et al. developed a series of poly(2-cinnamoylethyl methacrylate) (PCEMA)-based amphiphilic BCPs, including poly(tert-butyl acrylate)–PCEMA (PtBA–PCEMA) and PS–PCEMA–PtBA, which can self-assemble into well-ordered nanostructures such as micelles, nanofibers [88–91]. These nanostructures can further be used as nanotemplates for the preparation of organic/inorganic hybrids by selectively reducing the metal precursors into metal NPs in a specific region. Usually, various metal NPs such as CdS, Pd, or Fe3O4 NPs can selectively be introduced into the PAA region after hydrolysis of PtBA owing to the interaction between metal precursors and PAA. Moreover, owing to the presence of curable functional groups of PCEMA, various hybrid nano/micro-structures, including micelles [92], one-dimensional chain [93], can be fixed permanently by using UV irradiation to solidify PCEMA region, which show good stability in solvents and are well dispersed in water, posing great potential in bio-applications.

Besides, Liu et al. created one-pot synthesis method of hybrid micellar aggregates based on simply ligand exchange [94]. In this case, the Co NPs were prepared via high-temperature reduction of Co(II) by dodecanediol using trioxylphosphine (TOP) as the cosurfactant. Meanwhile, PS–PAA was used to replace the oleic acid on the surface of Co NPs, obtaining the BCP-coated NPs. Importantly, this BCP-coated Co NPs were readily cast into mechanically robust films, which may find applications in electric devices, electromagnetic shielding, and information storage.

3. Factors governing precise localization of NP in micelles

Tuning the dispersion and position of NPs within micelles is critical to optimize new optical, magnetic, and mechanical properties and is intrinsically difficult due to their strong enthalpy incompatibility (∆HNP–polymer) of the NP with polymer, long distance van der Waals attractions between the NPs (∆GNP–to–NP), and the conformational entropy loss of the polymer (∆Spolymer) resulted from polymer chain deformation induced by the insertion of NPs [44,55]. Inspired by well-established polymer degrees of freedom, spherical NPs have positional degrees of freedom (∆SNP–position), and shape anisotropy NPs have additional rotational degrees of freedom (∆SNP–orientation) [96]. The overall change of Gibbs free energy can be described using the equation below:

\[
\Delta G = \Delta H_{\text{NP–polymer}} + \Delta G_{\text{NP–to–NP}} - T \left( \Delta S_{\text{polymer}} + \Delta S_{\text{NP–position}} + \Delta S_{\text{NP–orientation}} \right)
\]

(1)

To avoid aggregation of NPs in the polymer micelles, one must reduce NP–NP attraction and employ strong favorable interactions between NPs and the host polymers to offset the entropic penalty associated with this process. Furthermore, to control the spatial arrangement of NPs in the micelles, one must minimize ∆SNP–position and ∆SNP–orientation to get ordered structure. To do so, a big issue is how to design and prepare the functional nanostructures by finely controlling the above factors, including surface chemistry, size effect, volume fraction of NPs, NP shape matter, and others, which will be addressed in the following parts.
3.1. Surface chemistry of NPs

The important factor in determining the stable incorporation of the NPs within a BCP matrix mainly lies in the compatibility of the NPs with the BCP microstructures, which in turn can be controlled considering the symmetry of both the inclusion and the BCP host. A commonly used method is to modify NPs with polymer brushes that favorably interact with polymer host and reduce the NP–NP attractive interactions. Also, the uniform dispersion of NPs in polymer micelles is mainly determined by whether the brushes on the NPs are wetted by the host polymer. Specifically, NPs modified with homopolymers with varied molecular weight [97,98], different grafting density [99], different chemistry, mixed polymer brushes [100,101] or even BCP with same or similar to the host BCP can significantly affect the distribution and localization of the NPs in the micelles. Chemically anchoring polymer chains on the particles can be achieved through well-known Brust–Schiffrin synthesis or ligand-exchange approach [102].

Li et al. have demonstrated that Au NPs could be modified with a mixture of hydrophilic and hydrophobic ligands by ligand exchange route [103]. Variation of NPs ligands and processing methods allow them to disperse Au NPs either within one of the microdomains, or at the interface between the microdomains. This confirms that surface modification on the NPs can tailor ligand–polymer and ligand–surface interactions, allowing one to control the orientation and spatial organization of the NPs arrays simultaneously in BCP assemblies. Recently, Moffitt’s group prepared CdS QDs surrounded by mixed brushes of hydrophobic PS and hydrophilic poly(-methacrylic acid) (PMAA). Addition of water to THF solution of these NPs led to the formation of large micelles, in which the PS and PMAA brushes formed the cores and the coronas, respectively, leaving the QDs at the interfaces [104].

Moreover, Eisenberg et al. successfully incorporated Au NPs coated with PS270−PAA15 into only the central portion of PS190−PAA20 BCP cylindrical and spherical micelles [105], as shown in Fig. 7. To further control the NPs position in the BCP micelles, Chen and coworkers reported an approach for the synthesis of Janus-shaped hybrid colloid via the assembly of BCPs and NPs in the presence of hydrophobic (L\textsubscript{A}) and hydrophilic ligands (L\textsubscript{B}). The binding competition between L\textsubscript{A} and L\textsubscript{B} on the surface of NPs breaks the symmetry of surface attachments of BCPs of PS\textsubscript{154}−PAA\textsubscript{60} on the NPs. Both L\textsubscript{A} and L\textsubscript{B} are able to coordinate with the NPs, whereas comparing with L\textsubscript{B}, L\textsubscript{A} has a higher tendency to be embedded on the PS layer due to stronger hydrophobic interactions. Consequently, during the self-assembly, the BCPs preferred to associate with the surfaces of the NPs covered by L\textsubscript{A}, leaving the L\textsubscript{B}-attached surface exposed to water. The relative concentrations of L\textsubscript{A} and L\textsubscript{B} used for the self-assembly determined the morphology of the resulting NPs-hybrid colloids. When [L\textsubscript{A}]:[L\textsubscript{B}] varied from 1:0, 1:22, to 1:132, the core/shell morphology evolved from homocentric to slightly eccentric and then to highly eccentric.

Spherical Au NP thiolated polymer brush can be more easily dispersed in the PS matrix not only due to spherical shapes with high curvature on their surface, but also thiolated molecules form the strong binding and high grafting density to the Au surface via Au−S covalent bonding. Usually, conventional single homopolymer brushes can hardly form high grafting density (2.0 chains/\textmu m\textsuperscript{2}) on the NPs. Utilizing a bimodal/mixed grafting polymer brush design, with densely grafted short brushes to shield particle surfaces and sparsely grafted long brushes that favor the entanglement with matrix chains, Schadler and coworkers dispersed TiO\textsubscript{2} NPs in high molecular weight polymer matrices [106]. The mismatch of binary polymer brushes with different lengths on the surface of NPs was also used to effectively improve wetting of the brushes by surrounding mismatched polymers. Binary polymer brushes on NPs surface create additional void spaces to accommodate sufficient conformational freedom for the matrix polymer close to the NPs surface. This significantly improves the stable displacement of the NRs in polymer matrix [107].

Electrostatic interactions/hydrogen bonding interactions can also be used to selectively locate NRs into specific microdomains of BCP micellar aggregates, forming novel nanocomposites with complex ordered structures [38]. Pochan group and Winnik group prepared hybrid micellar aggregates by binding oppositely charged NPs to the corona of polymeric micelles through electrostatic interactions [65,66], as described in more details in Section 2.5. In this method, Au NPs can form periodic stripes pattern perpendicular to the cylinder axes.

3.2. NP size effect

Spatial distribution of NPs in BCP is also affected by the size of the particles, since sufficiently small particles disperse freely within the polymer matrix. The stretching effect required by the block phase to circumvent the particles is less significant for small-sized particles than for large-sized particles, and is also dependent on the nature of the NP–polymer interaction [108]. A simulation of the self-assembly of BCP/NP mixtures in solution, based on self-consistent-field and

![Fig. 7. Schematic illustration and the TEM images of incorporation of PS−PAA coated Au NPs into the central portion of BCP cylindrical and spherical micelles. The red color represents the hydrophobic PS composition (or the core in the cylindrical or spherical micelle), and the blue color expresses the hydrophilic PAA composition (or the corona in the cylindrical or spherical micelle, which cannot be seen in TEM images without staining). Reprinted with permission from Ref. [105].](image-url)
density functional theories, shows that small volume fractions or sizes of the particles would favor a random distribution in micelle core, while large volume fractions or sizes of the particles would prefer an interfacial localization driven by unfavorable mixing energies (e.g., from steric packing) [109]. Therefore, spatial distribution of NPs in the microphase-separated morphologies can be controlled by tailoring the NPs ligands (i.e., enthalpic effects) and the size of the NPs relative to the radius of gyration \( R_g \) of the host polymer (i.e., entropic effects) [49-110].

Some studies elucidated the influence of particle size on the number of encapsulated particles. Taton encapsulated a single Au NP into the PS core of each PS–P4VP micelle when the NPs were larger than 10 nm through co-precipitant route [47, 111]. For smaller NPs (\( \sim 4 \) nm diameter), multiple particles were encapsulated in each micelle, even at very low particle-to-polymer ratio. It was suggested that for small NPs \( (R_{NP}/R_g < 1) \), polymer chain adsorption is templated by the particle surface, leading to the encapsulation of a single particle and the formation of a concentric polymer shell around the particle [111]. However, this concentration is inapplicable to some other large NPs (\( >10 \) nm), for example, \( \text{Fe}_2\text{O}_3 \) NPs. In those cases, only micelles with multiple core-embedded NPs could be obtained, even at very low particle-to-polymer ratios [48].

Zhu and co-workers also demonstrated that spatial distribution of NPs in micellar core depends on NPs size [11]: large NPs \( (D/R_0 > 1) \), where \( R_0 \) is the radius of the NPs, particles behave like solutes dissolved within micelle cores, presumably to maximize their entropy; for larger NPs \( (R_{NP}/R_g > 1) \), polymer chain adsorption is templated by the particle surface, leading to the encapsulation of a single particle and the formation of a concentric polymer shell around the particle [111]. However, this concentration is inapplicable to some other large NPs (\( >10 \) nm), for example, \( \text{Fe}_2\text{O}_3 \) NPs. In those cases, only micelles with multiple core-embedded NPs could be obtained, even at very low particle-to-polymer ratios [48].

3.3. NP shape matters

Anisotropic NPs exhibit interesting properties that are sometimes more desirable than conventional spherical ones [114]. For example, NPs with irregular shapes possess plasmonic “hot spots” at high-curvature corners, which may demonstrate stronger plasmonic coupling between the particles than spherical ones. From a directed assembly point of view, anisotropic NPs face an additional challenge beyond the ones inherent in assembling isotropic particles. Their anisotropy in shape and possibly chemical composition, which gives rise to many of their unique properties, must be taken into account when assembling the particles. Unlike spherical NPs, anisotropic NPs tend to have complex behaviors and their assemblies involve more energetic considerations. NPs with different shapes have various facets on their surface, and different curvatures on their surfaces [115]. For instance, the NRs were capped with five (111) facets at the both ends, while the side surfaces were enclosed by (100) facets. CTAB preferentially binds to the (100) side-faces compared to the (111) faces. This could allow for the binding of thiol-terminated polymer more easily to the ends of the NRs [116]. Furthermore, compared to spherical end morphology, the relatively small surface curvature of the longitudinal side of NRs makes them more difficult to get high grafting density. This is because the “grafting to” method is a self-limiting process during which the polymer chains must diffuse through the existing grafted polymer chains to reach the reactive sites on the NP surface. Large surface curvatures on the surface could create more void spaces close to the NR surface. In this way, small spherical NPs could obtain high grafting density on their surfaces.

Theoretical and experimental studies have demonstrated that even when the brushes are chemically identical to the matrix, an unfavorable entropic interaction still remains, due to the so-called “autophobic dewetting” effect [117–119]. Zhu and coworkers described an approach to disperse and orient NRs within cylindrical BCP micelles by tethering brushes of same homopolymers with different lengths onto the surface of NPs (Fig. 8) [107]. Due to the mismatch of the different polymer brushes, additional void space would appear on the surface of the NRs, which will provide sufficient conformational freedom for the matrix polymers close to the NRs surface, improving the wettability of the brushes and polymer matrix. Cylindrical micelles provide two dimensional confinement, leading to parallel alignment of NRs to the long axis of the cylindrical micelle to minimize the entropic deformation of the BCPs and to overcome the rod–rod interaction (dipole–dipole and van der Waals interactions). The NRs organized end-to-end to form nanorings within the cylinders, which is consistent with computational results. Clearly, orientation freedoms of the NRs are strongly restricted in order to minimize the entropic penalty associated with the deformation of the PS chains around NRs when the length of NRs is increased due to the confinement from the cylinders.

NPs with other shapes, such as nanoplatelets [120], nanowires (NWs) [121], and nanodumbbells [122], can also be encapsulated into BCP micelles, which may produce novel and complex properties. For instance, triangular \( \text{La}_3\text{F}_7 \) nanoplatelets have been introduced into the \( \text{PS}_{404}\text{–PAA}_{22} \) micelles to form 1D stack aggregates (Fig. 9a). Otherwise, the nanoplatelets can stand vertically or pack horizontally on the polymer scaffold, which might bring anisotropic properties. Recently, Chen et al. successfully introduced Au NWs into BCP micelles and realized the coiling of metallic filaments (Fig. 9b) [121]. Each polymer micelle contains one circular spring-like coil of \( 5–10 \) loops. The mechanism of transformation from straight wires to circular rings results from the contraction of encapsulating polymer shells and energy minimization of the combined Au NW–polymer system. The release of the stored mechanical energy upon removal or swelling of the polymer shells can further prove the transformation mechanism. Compared to Au NRs, Au nanodumbbells can provide a steric factor, facilitating the NPs assembly into more complex structure. When more Au nanodumbbells are incorporated into the polymer micelles, they can form spherical clusters whose internal distribution is defined by packing of the dumbbell-like shape. Thus, steric hindrance provides a simple way to effectively tune the interactions between NPs and realize the fabrication of hybrid micelles with well-defined structures, as shown in Fig. 9c [122].

3.4. Kinetic control

BCP and NPs can self-assemble into three “classical” morphologies: spherical micelles, cylindrical micelles or vesicles when treated with selective solvents [123]. Simply mixing the alkane-covered NPs and BCPs leads to non-uniform particle clustering or aggregation, resulting from the fact that equilibrium state in the solution is hard to be achieved. However, complex nanostructures can be produced by taking advantage of this non-equilibrium dynamic process in co-assembly of NPs and amphiphilic BCPs [124]. Based on this, Park’s group achieved the dense packing of TOPO-coated QDs in the middle of the PS walls of PS–PAA vesicles [49].
They further presented an approach to radically locate QD NPs into the spherical interface between the polymer core and shell of BCP aggregates by finely controlling the interfacial energy of the composite system [30,110]. Three distinct structures, including polymersomes densely packed with NPs, core–shell type polymer assemblies where NPs are radially arranged at the interface between the polymer core and the shell, polymer micelles where NPs are homogeneously incorporated, can be obtained by employing three different common solvents. The different morphologies produced from different solvents could be attributed to solvent–polymer interaction. Depending on the degree of stretching for PS and PAA chains, it is predicted that the relative volume taken by PAA is smaller in dioxane than in DMF and THF, leading to the formation of vesicles in dioxane and micelles in DMF and THF. In addition, NP–PS interaction in system containing different common solvents strongly affected the NPs arrangement in the polymer matrix. PS has a relatively lower solubility in DMF than in THF and dioxane, leading to a compact PS core of the micelles prepared from DMF solution. As a result, NPs are pulled out of the compact PS cores and located at the interface between the core and the shell during the formation of the assemblies from DMF/THF. In contrast, THF or dioxane common solvents can swell the PS cores of the micelles, allowing NPs distribute throughout the polymer micelles or vesicles walls [30].

Interestingly, microfluidics processing has been used to continuous self-assembly of mixtures of hydrophobic NPs and amphiphilic BCPs or polymer-tethered amphiphilic NPs into various structures with controlled sizes and morphologies [125,126]. This strategy adopted hydrodynamic flow to control the kinetic aspects of the assembly process, thus achieving non-equilibrium structures [127]. The key to manipulate this self-assembly is to balance the competition of the mixing of solvents and the assembly kinetics of NPs. By

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**Fig. 8.** TEM images of PS–P4VP hybrid micelles containing Au NRs array with well-ordered structures. Au NRs were encapsulated into the cylindrical BCP micellar cores through directed supramolecular assembly route. NRs within micelles can be tuned to form one-dimensional nanostings with end-to-end organization of NRs along the micelles or with side-by-side twisted arrangement of NRs perpendicular to the micelles. Reprinted with permission from Ref. [107].

**Fig. 9.** (a, b) Schematic presentation showing the dimensions of individual LaF₃ triangular nanoplates and their stacks and TEM image of the coassemblies of triangular nanoplates and PS–PAA. (c) Coiled nanosprings embedded in PS–PAA micelles. (d) Encapsulation of gold nanodumbbells within polymeric micelles. Reprinted with permission from Refs. [120–122].
varying the flow rate of water and common solvent (e.g., THF) phases, Au NPs can assemble into a variety of nanostructures, including micelles, giant vesicles and disk-like micelles. Under microfluidics processing, fluid shear will affect the coalescence and breakup of the micelles, affecting the final morphologies [128,129].

In addition, Moffitt et al. reported the kinetic control of QDs loaded compound micelle particle size and chain stretching within the external PAA stabilizing layer via changes in the initial polymer concentration and rate of water addition. By increasing the initial polymer concentration or decreasing the rate of water addition for a constant blend composition (PS$_e$PAA and PS$_e$PAA stabilized QDs in DMF), larger hybrid particles were obtained. This method relies on the kinetic nature of hybrid size, which depends on a window of growth between the onset of self-assembly and the freezing of particles growth above the critical water concentration. The thickness of the external PAA layer is determined for various hybrid micelle sizes, showing that PAA stretching in the external brush layer increases with increasing the particle size, reaching the limit of fully extended chains for sufficiently large particles [130].

3.5. Morphology transition induced by NP addition

BCPs do not simply template the arrangement of the NPs, and they can also have an impact on the supramolecular structures of BCPs; incorporation of NPs has been found to lead to the morphology transition of parent BCPs [110].

Winnik et al. reported the morphological transition of hybrid spherical micelles to wormlike micelles due to shearing force. PS–P4VP forms spherical crew-cut micelles with a PS core and P4VP corona when 2-propanol is added to a solution of the polymer in chloroform. When the chloroform also contains CdSe QDs, hybrid micelles form with QDs bound to the corona. They reported that vigorous magnetic stirring of a solution of these hybrids micelles in a solution containing 73 vol% 2-propanol led to a morphology transformation to form 3D wormlike networks. Under the influence of shear, PS$_{40}$P4VP$_{75}$ micelles appeared to aggregate and then rearranged to form colloidal stable networks consisting of wormlike micelles, uniform in width, which were presented as loops and tails connected by T- and Y-junctions [131].

Incorporation of NPs with high loading in host polymer domain leads to high chain conformation entropic penalties and then drastically decreases the effective interaction parameter of each block. Zhu and co-workers demonstrated that hybrid spherical micelles can be transformed to cylindrical micelles and nanosheets when increasing the content of NPs from 14 to 57 wt%. (Fig. 10) [132]. The NP-driven sphere-to-cylinder and cylinder-to-nanosheet morphological transition can be attributed to the relative volume change between the PS and P4VP(PDP)$_{1.0}$ phase of the supramolecules [11,132]. The incorporation of NPs increases the effective volume taken up by PS phase, while the relative ratio of P4VP(PDP) microdomain decreases, favoring the formation of lamellae. Similar phenomena have been observed for the co-assembly of NPs and BCPs in solution processing [30].

In order to load NPs in the micelles with high density while keeping the same morphology, Zhu and co-workers recently employed supramolecular approach to direct the NPs in the micellar cores. The number of NPs in each spherical micelle can be effectively increased from 1 to ~80 by simply increasing the

![Fig. 10. TEM images of hybrid assemblies formed from PS$_{20k}$–P4VP$_{17k}$(PDP)$_{2.0}$ encapsulated of gold NPs (size: 7.5 nm) with content of: (a) $\phi_{NP} = 14.2\%$, spherical micelles with ~1 NP; (b) $\phi_{NP} = 33.1\%$, spherical micelles with ~2 or more NPs; (c) $\phi_{NP} = 49.7\%$, cylindrical micelles and small amount of spherical micelles; (d) $\phi_{NP} = 56.9\%$, dominating nano-sheets along with cylindrical micelles. $\phi_{NP}$ represents the volume fraction of the NPs in the micelles. Reprinted with permission from Ref. [132].](image-url)
content of NPs and adjusting the ratio of PDP to P4VP units accordingly. The balance between the PS-grafted NP loading (increasing the volume fraction of PS domain) and the PDP addition (increasing the volume fraction of PVP/PDP domain) maintains the same micellar morphology while achieving high NP loading. Moreover, strong enthalpic attraction of H-bonding between PDP and P4VP can increase the effective interaction parameter of the system to maintain the strong segregation, leading to the formation of ordered structures. The mass density of NPs in the hybrid micelles was further enhanced after removal of the added PDP from the supramolecules.

Lin et al. simulated the assembly of BCPs and NPs in selective solvent by combining self-consistent-field theory for fluids and density functional theory. The aggregate morphologies can be tuned by the particle radius and particle volume fraction. For the selective particles, the aggregate morphologies of the hybrid micelles can experience a transition from vesicles to mixture of circle like and rod micelles as the particle radius and/or particle volume fraction increases. For the nonselective NPs, the large compound micelles are produced instead of the vesicles [109].

4. Properties endowed with NPs and applications

4.1. Biomedical application

Polymer micelles offer a powerful multifunctional platform for drug delivery and diagnostic imaging applications. The hydrophobic micelle core provides an ideal nanocarrier compartment for hydrophobic agents, and the shell consists of a protective corona that stabilizes the NPs. Many hydrophobic drugs (e.g., paclitaxel and doxorubicin) have been successfully loaded inside the micelles core to improve drug solubility and pharmacokinetics.

Biological applications of hybrid micelles mainly depend on the properties of NPs encapsulated in BCP micelles. For example, QDs can be used to realize in vivo or in vitro imaging owing to their unique optical properties, including wideband excitation, narrow emission, phenomenal photostability, and high quantum yield [133,134]. Magnetic NPs can be used as MRI contrast agent for in vivo imaging and further realize the targeting function due to the directional movement under magnetic field [135]. However, inorganic NPs may have potential toxicity when used in vivo; thus, in order to solve that problem, BCPs have been used as protective carrier for delivery of the NPs into specific area in vivo, which can significantly improve the biocompatibility. In 2002, Dubertret et al. for the first time used phospholipid BCP to encapsulate QDs into core of micelles, enhancing the biocompatibility, which were injected into frog oocyte cells and realized the real-time tracking of embryonic development [24]. Recently, Shuai et al. developed novel multifunctional micelles for tumor-targeted intracellular drug release and fluorescent imaging by encapsulating anticancer drug paclitaxel and QDs into triblock copolymer PEG–poly(N,N’-diisopropylaminoethyl) aspartamide)–cholic acid (PEG–PAsp(DIP)–CA) micelles and introducing folic acid on the surface of micelles, as shown in Fig. 11 [136]. In order to realize targeting function by using NPs, magnetic NPs (such as Fe₃O₄ NPs) have been incorporated into biocompatible amphiphilic BCPs such as poly(lactic-co-glycolic acid)–PEG (PLGA–PEG) micelles, which not only can provide the imaging function, but also can drive NPs into the cancer cells under external magnetic fields, thus realizing the dual functions of imaging and targeting [28,137,138]. Another challenge in biomedical application is to realize the controlled release of drug in vivo when the micelles containing drugs have targeted to the cancer cells. Although pH and temperature triggered release of drug have been used in the last decade, it is hard to control the release condition in vivo. Recently, using near-infrared light to control drug release based on the photothermal effects of Au NR and Au nanocage provides a facile and robust way and poses significant potential in the future medical applications [127,139].

Recently, Liu et al. synthesized water-dispersible superparamagnetic polymer/γ-Fe₂O₃ composite micelles based on novel BCPs, PCEMA–PAA and poly succinated (glyceryl monomethacrylate)–PCEMA (PSGA–PCEMA). By controlling the synthesis condition, micelles with surface bumps (PSGA domains) could be obtained. More importantly, The PSGA domain could be used to immobilize bovine serum albumin (BSA) owing to the presence of carboxyl groups. The immobilized BSA retains its activity and binds with anti-BSA, which may open up a door for immunoassays [92].

4.2. SERS probes

Surface enhanced Raman scattering (SERS) is a surface-sensitive technique that enhances Raman scattering by molecules adsorbed on rough metal surfaces. SERS has been studied extensively on various substrates owing to the huge enhancement of the SERS signal, by a factor of ~10¹⁴–10¹⁵, which improves the detection limit from ensembles of molecules to the single-molecule level and can be used from fundamental research to medical applications [140]. The SERS mechanism comes from two major enhancements, e.g., the long-range electromagnetic (EM) enhancement and a short-range chemical enhancement, which result in an increase in the Raman scattering cross-section of the adsorbed molecules.

Generally, Au NPs have been used widely as SERS substrates to probe components in bio-environments. Some small molecules have been used to coat on the surface of Au NPs as Raman reporter, which act as the source of enhancement. By comparison with the fluorescent labels, one of the advantages of Raman reporters on metal NPs is effectively to avoid photo-bleaching. Another advantage is that multiple Raman reporters can be excited with a single light source such as near infrared light. Direct attachment of Raman reporters onto metal NPs lack the efficiency and reliability of the nanoprobe; thus, some materials, including biomolecules, polymers, or inorganic layers have been introduced to coat Au NPs and improve the stability of the nanoprobe. Thus, hybrid micelles consist of Au NPs and Raman reporter (such as 2-naphthalenethenyl) have been prepared by using heating and cooling method based on PS–PAA (Fig. 12a) [141]. The polymer shells can protect the encapsulated nanoprobe, which will be beneficial for applications in adverse conditions. The enhancement factor (EF) of nanoprobe can be increased significantly by increasing Au NP diameter and density. It is demonstrated that the relative Raman intensities of dimers and trimers are 16 and 87 times than that of hybrid micelle containing single Au NP, respectively (Fig. 12b) [142]. More importantly, a wide variety of reporters could be incorporated into the polymer micelles by this encapsulation method for realization of multiplexed detection of target molecules.

4.3. Catalysis

Another promising application for inorganic/polymer hybrid colloids is to develop catalysis with special catalyzing behavior in reactivity, stability and selectivity [143,144]. Zhang et al. synthesized Au NPs inside the core of thermoresponsive micelles of poly(N-isopropylacrylamide)–P4VP (PNIPAM–P4VP) [145]. Temperature responsive solubility of PNIPAM corona chains was used to adjust the catalytic activity. Below low critical solution temperature (LCST), the PNIPAM chains were hydrophilic and extended which exposed the Au NPs to the hydrophilic reactions and accelerated the reactions. On the other hand, above LCST, the solubility of PNIPAM
chains decreased and the Au NPs were covered by the collapsed PNIPAM chains, which decelerated the reaction.

In addition, PS–PAA spherical micelles encapsulation of Au NP dimmers were prepared through the heating–cooling approach. This hybrid micelles can be used as catalyst and offer a unique opportunity to use the organization of Au NP to guide the growth of ZnO NWs [144]. Au NP dimmers could be enriched to ~60% by repeated centrifugation method, which can be used to catalyze the

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Fig. 11. (a) Illustrative preparation of PTX and QD-loaded micelles and pH-tunable drug release. (b) In vivo QD fluorescence images showing folate-enhanced tumor targeting of the QD-loaded targeted micelles after tail vein injection into nude mice bearing Bel-7402 subcutaneous xenograft (dose: 70 mg micelle/kg body weight).

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Fig. 12. (a) Schematic illustration of preparation of hybrid micelles composed of Au NPs and Raman reporters such as 2-naphthalenethiol by using heating–cooling method. (b) SERS spectra of the hybrid micelles enriched with (a) monomers, (b) dimers, and (c) trimers of Au@Ag NPs (d = 20 nm; excitation: 785 nm at 290 mW; insets: the histograms of these samples). The schematics in the lower panel show the SERS intensity ratio of the nanoclusters.

Reprinted with permission from Refs. [141,142].
growth of semiconductor NWs through a vapor liquid solid process. The hybrid micelles were dispersed on sapphire substrates and the ZnO NWs can grow epitaxially on the crystallographically compatible sapphire substrates at \( T \approx 800 \) \( \text{°C} \) induced by the catalytic action of Au NPs. NW dimmers with narrow spacing (20–60 nm) can be achieved and dimeric NW population reached \( \approx 25\% \), which may have potential to create new electrical and optical properties.

4.4. Artificial atoms or building blocks for secondary assembly

Hybrid micelles with encapsulated NP can serve as building blocks for further self-assembly. For example, spherical micelles containing single Au NPs can be used as ‘organic monomers’, which occur to polymerize into one-dimensional chain structure upon acid treatment, similar to the chain-growth reaction in polymer chemistry (Fig. 13a–c) [146]. By controlling the swelling of PS domains (i.e., adjusting the solvent ratio), single-line chains of up to 300 Au NPs in length were also synthesized. Moreover, the pre-fabricated single-line chains can be converted to double- or triple-like chains, indicating the critical role of PS-solvent interfacial tension in restricting the width of the chains.

Furthermore, spherical micelle can be transformed into wormlike micelles by simply controlling the formation conditions (Fig. 13d–f) [147]. In this case, the above morphology transition can be realized when immersing the hybrid micelles with crosslinked shell into the aqueous solution of NaCl, CaCl\(_2\), acetic acid (AcOH), or EDC. With the increase of Au NPs in wormlike micelles, their aqueous suspension will change color from reddish to paler, bluish violet, resulting from aggregation of the gold NPs and coupling of surface plasmon excitations. When the salts and acid are used to form wormlike micelles, the morphology can return back to the initial state (spherical micelles) by neutralizing or diluting the additive. On the other hand, the permanent wormlike micelle can be obtained by using EDC and diamine linker simultaneously. By controlling the shell thickness, the NPs spacing of wormlike micelles can be tuned precisely.

Above a critical size, Co NPs aggregate into chains because of magnetic dipole–dipole interaction. Based on this principle, individual hybrid micelles containing Co NPs can easily form wormlike micelles [93]. In this case, the Co NPs were prepared from the high-temperature decomposition of Co\(_2\)(CO)\(_8\) using PCEMA–PAA as surfactant. After that, PtBA–PCEMA was used to coat Co NPs chains and occur to crosslinking by using UV irradiation owing to the curable functional groups of PCEMA, resulting in the preparation of permanent hybrid wormlike micelles.

5. Summary and outlook

In this paper, we have reviewed recent advances in the field of hybrid BCP micelles containing various preformed inorganic NPs. BCP can self-assemble into well-defined microphase-separated morphologies, which can be used as templates to guide NPs assembly. On the other hand, compared to in situ synthesized NPs in BCPs, preformed NPs not only can offer their unique properties, but also can realize the precise control of NP position in BCP nanocomposites. Taking the advantages of BCP and inorganic NPs, various hybrid polymer micelles with different shapes, properties, and functions have been developed in the last decade, which
have been used in various fields such as biomedical area (imaging, detecting and targeting), optics, electric, etc. We have discussed various strategies developed in the past few years, which aim to rationally design the structure, properties and functions of hybrid BCP micelles. Specifically, we have highlighted newly-developed methods, which allow to precisely control the localization of NPs in BCP micelles. Finally, various applications associated to these hybrid micelles with encapsulated NPs have been outlined.

Up to now, most of research based on hybrid BCP micelles containing preformed NPs focused on the simple encapsulation and uniform dispersion of NPs. More recently, much attention has been paid to distribution, orientation, and assembly of NPs in BCP micelles, which will open up a door for the development of advanced functional nanocomposites. Although some progress has been achieved, the studies on precise control of NPs position in BCP are still in the initial stage. There are a lot of problems or challenges that should be addressed in the future. The first is to design and prepare novel types of BCPs or NPs with more desired structures that suitable for encapsulation. In this case, copolymers with hyperbranched and star structures, BCPs containing inorganic elements, crystalline or biodegradable components will enrich the phase structure and morphologies to a large level. On the other hand, NPs with various shapes such as nanotubes, nanocubes, nanoshells, nanohexapod, etc, or different compositions, not only will produce new properties, but also will be a novel kind of building block for fabrication of 3-D assembly of NPs. For the second aspect, new types of strategies should be explored to realize the orientation, location, and ordering of NPs in BCP micelles. For instance, precise control of NPs in 1-D or 2-D has recently been achieved by using supramolecular assembly method; however, publications on arranging NPs into 3-D well-ordered structure in BCP are still limited. Otherwise, cooperative assembly of various kinds of NPs in BCP micelles is important for realizing the combined properties and integrative performances, which is still one of the challenges. Finally, since the development of device offers us one of future directions, whose properties and performances are largely dependent on the structural complexities; thus, hybrid micelles with complex structures might be further used as building block for realization of the 3-D assembly with highly hierarchical structures from nano-scale to macro-scale. New collective properties can emerge by confining nanoscopic inclusions to narrow regions within the microstructures. Gradient materials with larger NPs located in the center while small NPs located at the interface will result in unusual optical and electrical properties [148].

External forces, including electrical, magnetic, shearing and thermal fields can also be helpful in manipulation of NPs in co-assembly. We anticipate that the spatially defined organization of functional NPs in BCPs will provide new opportunities for studying the complicated photophysics intrinsic to blends of nanoscale systems, such as bulk heterojunctions, which are characterized by electronic interactions at interfaces rather than between specific donor–acceptor molecules.

Besides, there are still other fundamental research that should be exploited, such as the enthalpic and entropic effect on the self-assembly processes, which will bring us to the upper level of understanding for the fabrication of BCP-based devices based on hierarchical NP arrays. Combination of BCP and NPs has posed a great potential for the future developments, considering the complex system; thus, there is still a long way to go, interdisciplinary research might lead to the new breakthrough in the further development of hybrid BCP micelles. The challenges involve exploration of new controllable assembly strategies, deep understanding of structure–property relationships to predict the performance of a given structure, and creation of systematic theories.

With these advances, precise localization of NPs in BCP aggregates of controllable morphologies holds promise for fabrication of functional materials with tailored structures, functionalities, and applications. We hope that one can obtain some inspiration from this feature article, and push the further work to the bright, e.g., next-generation optoelectronic or sensing device.

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References

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