A one-pot approach using recyclable template to prepare dual-responsive yolk–shell or Janus-like nanoparticles†

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Herein, we report a one-pot approach using polymeric micelles as the recyclable template to prepare hybrid yolk–shell or Janus-like nanoparticles (NPs). The micelles were formed by a block copolymer PEG-b-P4VP (EV) in a methanol/water (1/9, v/v) mixture with PEG as the shell and P4VP as the core. In the mixture of the micelles with AIBN (azobisisobutyronitrile), HAuCl4, NIPAM (N-isopropylacrylamide) and MBA (N,N’-methylenebisacrylamide), hybrid NPs could be obtained by simply heating the mixture at 76 °C. At this temperature, AIBN that was largely localized within the hydrophobic P4VP core decomposed into radicals, which reduced HAuCl4 to form Au NPs within the core and initiated the copolymerization of NIPAM and MBA at the core–shell interface to form a poly (NIPAM-co-MBA) network (PNM) to cover the core. The micelle template was conveniently removed from the hybrid NPs by decreasing the pH value of the medium to 3.0. At a low pH, the P4VP block chains were fully protonated; thus, EV becomes highly hydrophilic and soluble in the medium. Moreover, the micelle template dissociated and then gradually diffused into the bulk solution phase as individual EV chains. After the removal of the micelle template, Au@void@PNM yolk–shell NPs were formed. However, when the EV micelles (with the core being slightly noncovalently crosslinked) were used as the template, the same process resulted in the Janus-like NPs; moreover, the micelles were recyclable. After the yolk–shell or Janus NPs were separated by centrifugation, the micelles were recovered in the supernatant and then used again as a template for additional cycles of the yolk–shell or Janus-like NPs preparation and the same results were obtained.

Both the yolk–shell and the Janus NPs were easily redispersible in water, and they were confirmed to have both thermal sensitivity and photo sensitivity. We believe that the facile and cost-effective preparation of the yolk–shell NPs (with dual sensitivities) and the Janus NPs (with a relatively high structural regularity) by localizing the chemical reactions within different nanodomains of the micelles should generate considerable interest in the fields of polymer chemistry and soft materials.

Introduction

Hybrid nanoparticles (NPs) have attracted increasing research interest in the last few decades because they can integrate the properties and functions of both inorganic and organic components. Moreover, from hybrid NPs, one can expect new features that were absent in either of the original ingredients. Hybrid NPs showed superior performances in the fields of energy storage,2 biomedical,3,4 contaminant removal,5 catalysis,6 etc.7

Of all the hybrid NPs, yolk–shell NPs (YSNs) have been of great interest in the fields of highly efficient catalysis,8 drug delivery,3,9,10 energy storage,11 etc. For example, in the field of catalysis, the core materials act as catalysts, the void spaces load reactive components and host the reactions, and the shell protects the catalysts from aggregation. As drug delivery vehicles, the voids supply a relatively large space for drugs, whereas the cores can provide binding sites and respond to stimulating environments to control the release of the payload drugs. The shell is capable of protecting and stabilizing the loaded drugs and affording the functionalities including biocompatibility and targeting. The void space also buffers the volume expansion during the charge–discharge cycles when the yolk–shell nanoparticles are used as the electrode
materials. Despite the superior features and wide applications, the current preparation approaches to YSNs mainly depend on the selective etching of regular core–shell NPs or sacrificial template, which are engineering-intensive or-and cost-ineffective.

Hybrid Janus NPs are another type of hybrid NPs that are very promising in the fields of hierarchical self-assembly, surfactants, catalysis, chem- or bio-sensors, and biomedicines. To date, the synthetic methods for the preparation of hybrid Janus NPs include phase separation, selective surface modification, microfluidic synthesis, electrified co-jetting, directed synthesis, and directed self-assembly. These synthetic strategies normally require the fine tuning of the structures or complicated multi-step processing. However, the methods reported for the preparation of hybrid Janus NPs with a size of ten nm are limited.

Recently, an important progress has been made in the field of preparation of hybrid nanomaterials using polymeric core–shell particles as a template. In particular, the use of unimolecular micelles formed by star-like and bottlebrush-like block copolymers resulted in a large variety of monodisperse nanomaterials. Herein, we report a facile one-pot approach to prepare hybrid yolk–shell NPs and Janus NPs using block copolymer micelles as the recyclable template. As depicted in Scheme 1, the micelles (with PEG as the shell and P4VP as the core) were formed by PEG-b-P4VP in a methanol/water (1/9, v/v) mixture. In the mixture for preparing the hybrid NPs, azobisisobutyronitrile (AIBN) is mainly encapsulated in the core because it is solvophobic, whereas N-isopropylacrylamide (NIPAM, the monomer) and N,N'-methylenebisacrylamide (MBA, the crosslinker) are solubilized in the bulk phase because they are solvophilic. HAuCl₄ is mainly located in the core such that it can interact with the pyridine units in the core. At a high temperature (76 °C), AIBN decomposes into radicals. Since AIBN is mainly located in the core, the radicals reduce HAuCl₄ to form Au NPs in the core, and thereby initiate the copolymerization of NIPAM and MBA at the core–shell interface to form a poly(NIPAM-co-MBA) network (PNM). As the PNM is solvaphobic at high temperatures, it aggregates at the interface and forms an integrated shell covering the core surface. After removing the template by simply decreasing the pH of the medium to 3.0, YSNs with both thermo- and photo-sensitivities and a structure of AuNP@void@PNM were obtained. In this case, the nucleation and growth of the AuNP occurs in the central area of the core. The position of the nucleation and growth of AuNP can be remarkably changed. Before the reduction of HAuCl₄, when the core is slightly non-covalently crosslinked, the nucleation and growth were excluded at the core/shell interface, and thus Janus-like NPs were produced. In each case, the micelles can be conveniently recovered and reused as the template for preparing the YSNs or the Janus NPs.

**Experimental**

**Materials**

Dichloromethane (CH₂Cl₂, 99.6%) and triethyl amine (TEA) were purchased from Sinopharm Chemical Reagent Co. Ltd and each of them was purified by distillation under atmospheric pressure after stirring the mixture with calcium hydride (CaH₂, Sinopharm) overnight just before use. Isopropanol (Aldrich, ≥99.7%) and 4-vinylpridine (Aldrich, 100 ppm hydroquinone as inhibitor, 95%) were purified by distillation under reduced pressure after dried by stirring the mixture with CaH₂ overnight. Poly(ethylene oxide)methyl ether (PEG113-OH, Mₙ = 5000, Mₘ/Mₙ = 1.02, Aldrich) was dried overnight under vacuum at 65 °C before use. Cuprous chloride (CuCl, 98%, Sinopharm) was firstly dissolved in a concentrated hydrochloric acid (CaH₂, Sinopharm) overnight just before use. Isopropanol (Aldrich, ≥99.7%) and 4-vinylpridine (Aldrich, 100 ppm hydroquinone as inhibitor, 95%) were purified by distillation under reduced pressure after dried by stirring the mixture with CaH₂ overnight. Poly(ethylene oxide)methyl ether (PEG₁₁₃-OH, Mₙ = 5000, Mₘ/Mₙ = 1.02, Aldrich) was dried overnight under vacuum at 65 °C before use. Cuprous chloride (CuCl, 98%, Sinopharm) was firstly dissolved in a concentrated hydrochloric acid (36%–38%, Sinopharm) under stirring, and then precipitated with a large volume of distilled water. Afterwards, the white precipitate of CuCl was washed twice with acetic acid (GR, Sinopharm) and ethyl ester (AR, Sinopharm) followed by drying by washing the vacuum oven for 48 h, and then stored in a CaCl₂ desiccator before use. Azobisisobutyronitrile (AIBN, Sinopharm) and N,N'-methylenebisacrylamide (MBA, Sinopharm) were purified by recrystallization in ethanol (AR, Sinopharm) twice followed by drying in a vacuum oven, and then stored in a refrigerator before use. N-Isopropylacrylamide
(NIPAM, TCI) was recrystallized in the mixture of toluene and cyclohexane (Sinopharm, v/v, 40/60) to remove the polymerization inhibitor followed by drying in a vacuum oven, and then stored in a refrigerator before use. All other materials were purchased from Sinopharm Chemical Reagent Co. Ltd and used as received.

**Synthesis of block copolymer PEG-β-P4VP**

PEG-b-P4VP (EV) used in this work was synthesized by an atom-transfer radical-polymerization of 4-vinyl pyridine using PEG-Br as the macrorinitiator based on the reported process (detailed process presented in Fig. S1†). The as-prepared block copolymer had the molecular formula of PEG₁₁₃–β–P₄VP₇₅ characterized by ¹H NMR and $M_w/M_n$ of 1.1 by GPC (Fig. S2 and S3†).

**Preparation of the micelle template**

The micelle template was prepared by a common solvent–selective solvent method. Specifically, PEG-b-P4VP (25 mg, 0.002 mM) and AIBN (8 mg, 0.05 mM) were mixed in 5 mL methanol in a 25 mL vial with magnetic stirring for 6 h. Deionized water (10 mL) was then injected into the vial through an injector pump at the speed of 1 mL h⁻¹ after which the opalescence appeared. The as-prepared suspension was transferred to a 50 mL volumetric flask and further diluted to the abovementioned supernatant containing recovered PEG-β-P4VP again, which were used for an additional two cycles of the YSNs or Janus NPs preparation.

**Fabrication of AuNP-PNM hybrid Janus NPs**

Sodium tetrachloropalladate(II) (73.55 mg) was dissolved in 1 mL deionized water to prepare an aqueous solution of Na₂PdCl₄ with a molar concentration of 0.25 M. Then, 1 μL aqueous solution of chloroauric acid at 0.25 M, 1 μL aqueous solution of sodium tetrachloropalladate(II) at 0.25 M and 5 mL micelle suspension at a polymer concentration of 0.5 mg mL⁻¹, were mixed in a 10 mL round bottom flask according to the molar ratio of HAUcl₄ : Na₂PdCl₄ : 4VP = 1 : 1 : 60, for a further 12 h of magnetic stirring under sealed conditions. The following procedures were exactly the same as those for preparing AuNP@void@PNM YSNs. Herein, the finally obtained wine-red pellet was AuNP-PNM hybrid Janus NPs, and the supernatant was collected for next round of preparation of the hybrid NPs.

**Fabrication of AuNP-PNM hybrid Janus NPs**

Four mg AIBN was dissolved in 100 μL methanol to prepare the methanol solution of AIBN at a concentration of 40 mg mL⁻¹. Then, 20 μL of the AIBN solution (containing 0.8 mg AIBN) was mixed with 2 μL chloroauric acid solution at 0.25 M (or, in the case of preparing AuNP-PNM Janus NPs, 1 μL chloroauric acid at 0.25 M and 1 μL sodium tetrachloropalladate(II) at 0.25 M). Subsequently, the mixture was added to the abovementioned supernatant containing recovered PEG-b-P4VP followed by 5 h of stirring. After adjusting the pH to 7 by adding NaOH, the mixture changed from transparent to opalescent. Characterization confirmed the formation of the PEG-b-P4VP micelles again, which were used for an additional two cycles of the YSNs or Janus NPs preparation.

**Characterizations**

Centrifugation was conducted using a ZhiZheng GL-21R high-speed frozen centrifuge. Hydrodynamic radius data was measured with an ALV-5000/E laser-scattering equipment with an incident wavelength of 632.8 nm. The sample morphologies were obtained by transmission electron microscopy (Philips CM120). The XRD patterns were collected on X'pert PRO (Cu Kα = 0.15406 nm). The UV-vis spectra were obtained by SHIMADZU UV-2550 UV-vis spectrophotometer.

**Results and discussion**

The micelle template

The fabrication of hybrid NPs started with the preparation of the PEG-b-P4VP micelle template encapsulating AIBN in its core. In the suspension of the template, the concentration of polymer is 0.5 mg mL⁻¹, the concentration of AIBN is 0.16 mg mL⁻¹, and the methanol/water volume ratio is 1/9 (see also the Experimental section). The average hydrodynamic diameter $<D_h>$ of the as-prepared micelles was measured by DLS and was found to be ~70 nm with a polydispersity index (PDI) of 0.1 (Fig. 1a). A TEM image of the micelle template is shown in Fig. 1b and its mean diameter was determined to be ~26 nm, which is much smaller than that measured by DLS
due to an invisible PEG shell in the TEM images and contraction of the micelles in the dry state.29

**Formation of the AuNP@micelle@PNM structure**

According to our previous study, in the suspension of the micelles in the methanol/water (1/9, v/v) mixture, a large part (more than half) of AIBN was located in the core of the micelles.26 It is possible that as the concentration of the micelles is very low, the concentration of AIBN in the core of the micelles is much (more than three order of magnitude)25 higher than that in the bulk solution phase. Moreover, in the mixture of micelle/AIBN/NIPAM/MBA/HAuCl₄, a considerable part of the HAuCl₄ molecules exist in the core due to complexation with pyridine units of the P4VP block chains.27,28 When the mixture was heated to 76 °C, AIBN decomposed into radicals. Due to the high concentrations of AIBN and HAuCl₄ in the core, the radicals reduced HAuCl₄ to form AuNPs within the core and initiated the copolymerization of NIPAM and MBA at the core–shell interface of the micelles to form the poly-(NIPAM-co-MBA) network (PNM) surrounding the core.26 This was revealed by an increase in the \( <D_h> \) from \( \sim 70 \) nm to \( \sim 104 \) nm (Fig. 2b). In the TEM image (Fig. 2a), the particles have an average size of ca. 45 nm, confirming growth in the particle size after the chemical reaction compared to 29 nm in Fig. 1b. The increase in the particle size was due to the formation of AuNP@micelle@PNM; the formation of both the AuNPs and the PNM resulted in an increase in size. The XRD pattern (Fig. 2c) indicated the formation of crystallized AuNPs with three diffraction peaks corresponding to (111), (200) and (311) crystal planes of Au. TEM image confirmed that the AuNPs are located in the central area of the hybrid NPs and the peripheral area with a relatively low contrast contains the polymeric components (Fig. 2a close up). The reason why only one AuNP was formed on the core–shell interface is that the radicals produced by the decomposition of AIBN are a weak reductant; therefore, the nucleation process is considerably slow.30

**Formation of the hybrid Janus-like nanoparticles using the micelle template**

In case of both HAuCl₄ and Na₂PdCl₄ being added, when heated at 76 °C, Au was reduced first (redox couples Au³+/Au and AuCl₄⁻/Au have higher electrode potential (standard hydrogen electrode, SHE, V) than Pd²⁺/Pd and PdCl₄²⁻/Pd, 1.498 V and 1.002 V compared to 0.951 V and <0.951 V).31 Moreover, during the nucleation and growth of Au NPs, the core is noncovalently crosslinked by the unreacted PdCl₄²⁻ acting as a cross-linker due to complexation between Pd and P4VP.28,32 Obviously, due to the crosslinking, the nucleation and growth of AuNP at the central area of the core was restricted. However, the nucleation and growth of AuNPs occurred at the core/shell interface of the micelle because the place is uncrosslinked at the area closest to the core, where the Au source is largely located.

**Formation of the hybrid YSNs and Janus-like nanoparticles obtained after the removal of micelle template**

By adjusting the system pH to 3.0, the P4VP block chains were fully protonated and became soluble in the medium. As a result, at pH 3.0, the micelle template dissociated into individual polymer chains that diffused into the bulk solution phase as individual chains; the template was thus removed from the hybrid NPs. After removal of the template, in the case when only HAuCl₄ was added and after removing the micelle template, AuNP@void@PNM yolk–shell NPs (YSNs) were obtained (detailed explanation of the structure is given below). The suspension was centrifuged and the YSNs were obtained by collecting the precipitates at the bottom of the centrifuge tube, which were re-dispersed in 2 mL of deionized water for further characterization by DLS and TEM and studies of the thermo- and photo-responses. The \( <D_h> \) of the YSNs was determined to be \( \sim 182 \) nm in diameter. The fact that the AuNP@void@PNM is remarkably greater than that of AuNP@micelle@PNM (104 nm) demonstrates that the PNM network further swelled after removing the template; the PNM network was, to a certain extent, entangled at the core–shell interface with the core of the micelles such that the swelling of the network was restricted before the dissociation of the core. After removing

![Fig. 1](image1.png)  
Fig. 1 The hydrodynamic radius distribution (a) and TEM image (b) of the micelle template.

![Fig. 2](image2.png)  
Fig. 2 TEM image (a), hydrodynamic radius distribution (b, compared to that of the original micelles), and XRD pattern (c) of AuNP@micelle@PNM particles.
the micelle template at room temperature, the PNM network was free to swell, leaving space between the AuNP and the PNM network; thus, the yolk–shell NPs AuNP@void@PNM were formed. According to TEM observations, the average size of AuNPs is 45 nm, which is much less than the \(<D_h>\) of the YSNs (\(\sim 182 \text{ nm} \)). In addition, the YSNs are much larger than AuNP@micelle@PNM (104 nm). These two facts indicate a large void size. However, in the TEM images (Fig. 3b), the size of the void observed is small. This should be caused by the remarkable contraction of the PNM in the dried state. Without staining, the PNM network is invisible in the TEM image. The content of the PNM network in the YSNs was determined to be \(\sim 80\%\) by TGA.

In case of both HAuCl\(_4\) and Na\(_2\)PdCl\(_4\) being added after the removal of the micelle template by adjusting the system pH to 3.0, hybrid Janus-like nanoparticles were obtained (Fig. 3c and d). By energy dispersive X-ray spectroscopy (EDS), we confirmed that the part with a high contrast was Au NP and no Pd element was detected in the hybrid Janus-like NP. The part with a low contrast is the PNM network. According to reports, the reduction potential of PdCl\(_4^{2-}\)/Pd is remarkably lower than that of AuCl\(_4^-\)/Au.\(^{31}\) Therefore, in the present study, the PdCl\(_4^{2-}\) was not reduced by the radicals. However, since the divalent PdCl\(_4^{2-}\) crosslinked the P4VP core, this makes the nucleation and growth of AuNP in the central area difficult. As a result, the nucleation and growth of Au NP was excluded to the core–shell interface, which is the place closest to the Au source and free for the nucleation and growth. However, the as-obtained Janus-like nanoparticles are not strictly biphasic NPs, where the surface of AuNP located at one side of the Janus nanoparticles is wrapped by a thin PNM layer, which prevents further aggregation between Au nanoparticles (Fig. S4†).

**Recycling of the block copolymer micelle template**

As mentioned previously, after the centrifugation step to separate the YSNs (or the Janus NPs), the hybrid NPs were precipitated and then collected and thus separated from the system. In the supernatant, the pH is 3.0, and the P4VP block chains of the PEG-\(b\)-P4VP block copolymer were protonated and molecularly solubilized. We then added the AIBN methanol solution and the HAuCl\(_4\) (or equal mole mixture of HAuCl\(_4\) and Na\(_2\)PdCl\(_4\)) aqueous solution to the supernatant followed by 5 h of stirring. After adjusting the pH of the supernatant to 7.0, the P4VP block chains were un-protonated and became insoluble in the medium; the PEG-\(b\)-P4VP micelles with the P4VP as the core and PEG as the shell were formed in the medium again, loading the AIBN in the hydrophobic core at the same time. After the addition of NIPAM and MBA, the process for preparation of the YSNs (or the Janus NPs) was repeated (Fig. 4).

The YSNs (or the Janus NPs) with a similar morphology and structure were produced. Again, the micelles were recovered and used as the template for an additional cycle of preparation of the YSNs or the Janus NPs, and similar results were obtained.

**Thermo- and photo-responsiveness of the YSNs**

To explore the potential applications of the as-obtained YSNs as a delivery vehicle for controlled drug release, their thermo- and photo-responsiveness were tested. As shown in Fig. 5a, the

![Fig. 3 TEM images of AuNP@void@PNM yolk–shell nanoparticles (a–b) and AuNP–PNM Janus nanoparticles (c–d).](image-url)

![Fig. 4 TEM images of the yolk–shell nanoparticles (a, b) and hybrid Janus-like nanoparticles (c, d) prepared using recycled micelle template.](image-url)
These nanoparticles have demonstrated the potential for use in medical applications, such as drug delivery systems. Their unique properties, including the rapid release of drugs upon exposure to heat or light, make them promising candidates for targeted therapies.

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Notes and references

Fig. 5 (a) Hydrodynamic radius distributions of YSNs at room temperature and under heat stimuli; (b) hydrodynamic radius distribution of YSNs at room temperature and under UV irradiation.


