Synthesis and applications of polymeric Janus nanoparticles

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1. Introduction

Research into Janus particles has received great attention over the past decade. In his Nobel lecture in 1991, Pierre-Gilles de Gennes suggested that asymmetric colloidal particles with different chemical compositions on the two lobes could have a special behaviour at interfaces, and named them "Janus grains.[1] Due to their asymmetry, Janus particles have the ability to offer more advanced chemical and physical properties compared to that of their symmetric homogeneous counterparts and in particular may behave as amphiphilic surfactants. However, for years after de Gennes' Nobel lecture, research into Janus particles was still slow, as evidenced by the limited number of publications in the field. The main limitations to the advancement of the field were the difficulty in synthesising well-defined Janus particles and also in characterising them, especially in the case of nanometer-sized Janus particles. From around 2005, the significance of Janus particles in a wide range of applications has become clear, including in surfactants, electrochemistry, catalysis, electronics, sensors, optics, superhydrophobic textiles and nanomedicine, and this has driven research to pursue different methods for the fabrication of Janus particles. In the past ten years, Janus particles have become a hot topic of research, as evidenced by the exponential growth in the number of publications in this area. Our latest search using the keyword “Janus particles” on Web of Science shows 1,608 published research papers on this topic which is more than 16 times higher than in 2010.

Several excellent reviews have been published in recent years addressing the most common synthetic methods leading to Janus particles.[2-5] This Chapter will review and discuss the main methods for the synthesis of Janus particles, and in particular, we will focus on the synthesis of both polymeric and hybrid Janus nanoparticles, with diameter in the nanoscale range. We will showcase a synthetic approach based on Reversible-Addition Fragmentation chain Transfer (RAFT) in seeded emulsion polymerization[6-8] which our group has been among the first to employ, together with the group of El-Aasser[9-10]. More recently other groups have been successful in similar approaches.[11-15] However, our group remains the first to be able to synthesise nanoscale polymer Janus particles by emulsion polymerisation, with typical particle size in the tens-to-one-hundred nanometers. The properties and potential use of Janus nanoparticles in a wide range of applications, derived from their asymmetric structure, will be reviewed and discussed.

2. Preparation methods

In this Section, we will describe the main synthetic approaches to date for the preparation of Janus nanoparticles. The synthesis of uniform Janus particles with well-defined geometry and size remains a major challenge, especially for the particles with diameter below 100 nm. From around 2005, the advancement in synthetic tools, including controlled polymerization techniques, has allowed different methods for synthesizing Janus particles to emerge. The methods most commonly used to synthesize Janus particles to date are grouped into three main categories: masking, self-assembly and phase separation, as shown in Figure 1.[4] In what follows, we will provide a critical assessment of these methods**.** When discussing the phase separation method, we will focus on the synthesis of polymeric Janus particle from seeded emulsion polymerization.

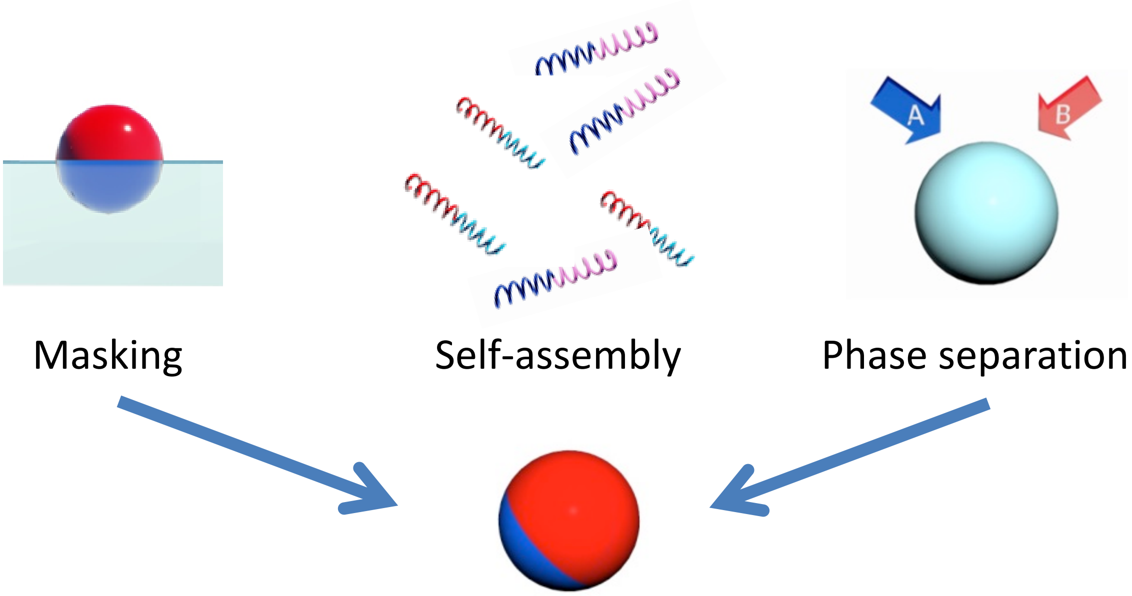

Figure 1. Schematic diagram illustrating three common strategies for the preparation of Janus particles: masking, self-assembly, and phase separation.

2.1. Masking

Masking is one of the first techniques that were used to synthesize Janus particles. The method involves the modification of only one side of the particle surface, while the other side is protected or masked. In 1988, Casagrande *et al.* first introduced the term “Janus bead” and used the masking method to describe glass spherical particles with diameter of 40-50 µm with one hydrophilic hemisphere and the other hydrophobic.[16] The authors investigated the use of the prepared Janus beads for their potential stabilization of oil/water emulsions and observed the different behaviour at oil/water interfaces compared to the precursor glass beads.[17] In general, the synthesis of Janus particles via masking process involves four steps, as shown in Figure 2: 1) homogeneous particles are trapped at the interface between two immiscible phases; one side of the particle is protected; 2) the other half of the particle at the interface is modified with desired properties; 3) the masking agent is removed; and (4) heterogeneous Janus particles are obtained. In this Section, we will review separately three examples of Janus particles prepared using a masking process with different immiscible phases, including liquid-liquid, liquid-wax hybrid, liquid-solid, and gas-liquid and gas-solid interfaces.

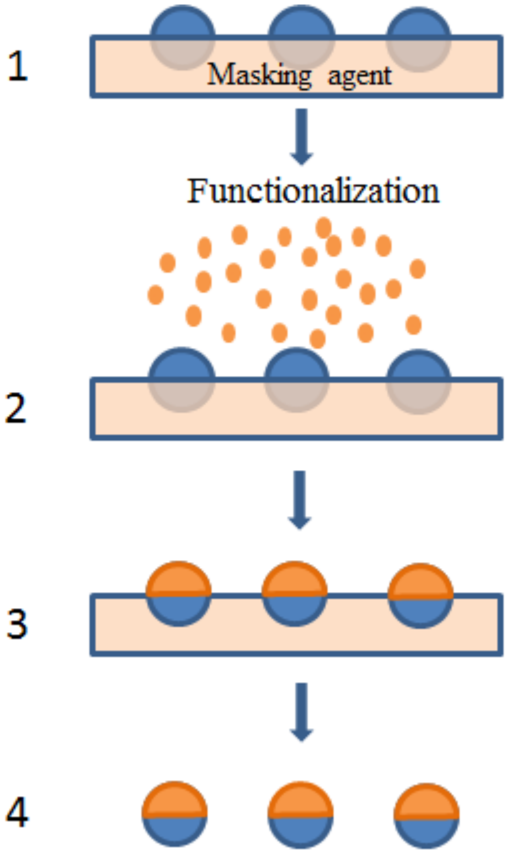

Figure 2. Schematic view of the synthesis of Janus nanoparticles via masking method.

2.1.1. Masking at a liquid-liquid interface

Asymmetric nanoparticles were obtained at the interface between two immiscible fluids. Gu *et al.* employed this strategy to prepare F_3O_4-Ag, FePt-Ag or Au-Ag hydrophobic Janus nanostructures.[18] As shown in Figure 3, these heterodimers made of two distinct nanospheres were prepared in two steps. First, oil-in-water Pickering emulsions were formed stabilised by F_3O_4, FePt or Au solid seed nanoparticles. Then catalytic reduction of a noble metal such as silver ions in the aqueous phase by Fe(II) on the seeds took place at the surface of the oil droplets. The prepared Janus nanoparticles could be functionalized through selective post-modification with different functional molecules to render them hydrophiclic which is useful for different biomedical applications including protein binding, bio-imaging and pathogen detection (Figure 3).[18] It should be noted that this approach has been only reported for nucleation of silver ions using aforementioned different types of nanoparticles as seeds.

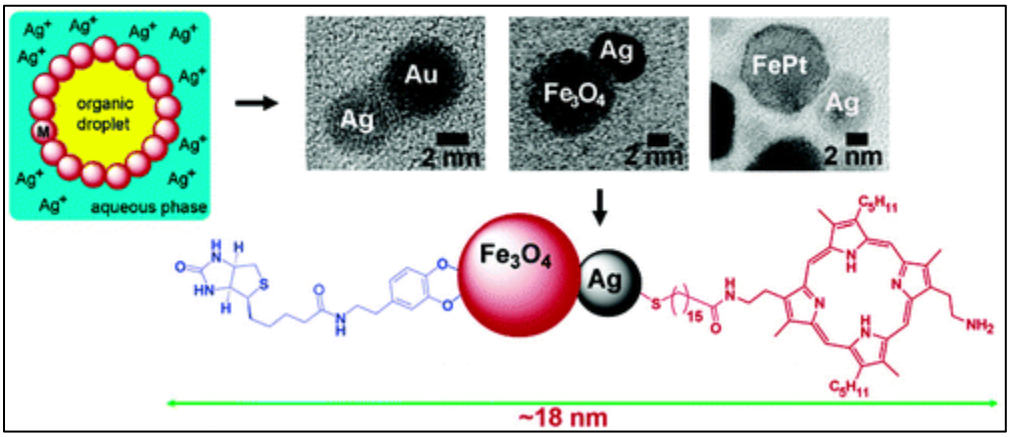

Figure 3. Synthetic scheme for functional heterodimers of nanoparticles formed at a liquid-liquid interface. Reproduced with permission.[18] Copyright (2005) American Chemical Society.

2.1.2. Masking at a liquid–wax hybrid interface

The Granick group prepared Janus particles using Pickering emulsion of paraffin wax droplets stabilized by silica particles at a temperature where the wax is molten.[19] The use of paraffin wax droplets as the dispersed oil phase is an interesting idea. The wax was easily solidified by cooling below its melting temperature, thus locking the particles at the wax-water droplet interface. These stable wax droplets were washed and the exposed surface of silica particles was chemically functionalized with silanes in organic solvents such as methanol. The Janus particles were then collected after adding chloroform to dissolve the wax (Figure 4). This method is relatively simple and cost effective to produce a relatively large quantity of Janus particles with distinct properties on each side. The main drawback of this method is that the particles could detach from the interface of the wax droplets during the chemical functionalization in the presence of organic solvents, thus leading to mixtures of Janus and homogeneous particles. The technique was later modified to a solvent-free method by the same group, in which the exposed surface of the particles was functionalized with silanes via vapour deposition.[20] Cui *et al.* used polydimethylsiloxane (PDMS) inert polymer film to create a liquid–solid interface. The exposed surface of the particles could be modified with metal, oxides or alloys such as silver, gold, nickel, and titania.[21]

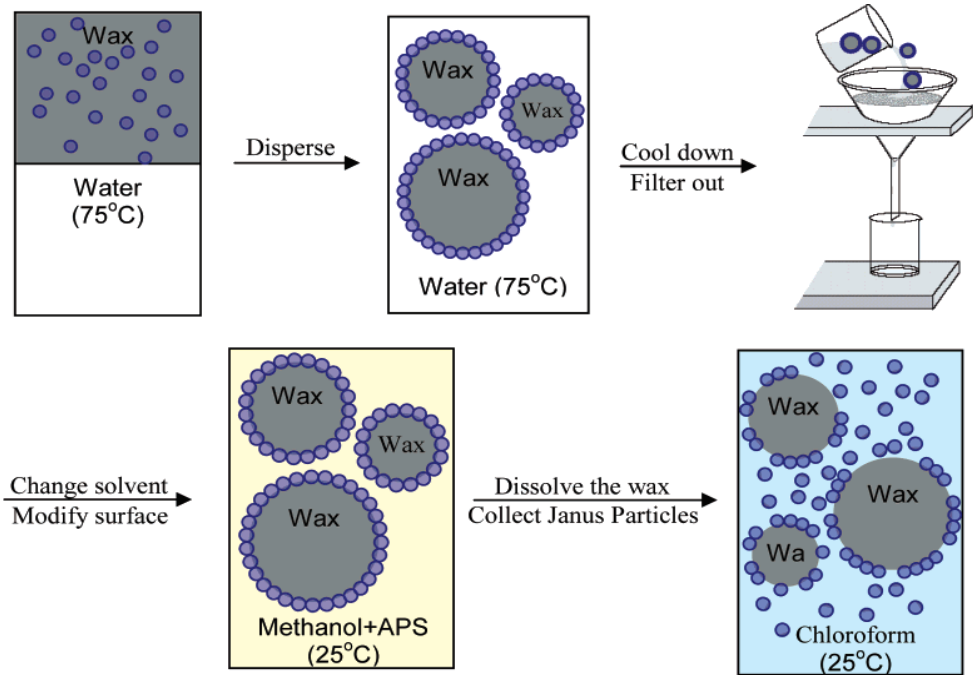

Figure 4. Schematic synthesis of Janus particles by functionalizing silica particles adsorbed onto an emulsion of paraffin wax in water. Reproduced with permission.[19] Copyright (2006) American Chemical Society.

This method was also employed by other groups to produce Janus silica particles with high yield. Liu *et al.* prepared acorn and mushroom shaped silica particles by introducing polymerizable vinyl groups onto the surface of the silica particles followed by the etching of the exposed surface with ammonium fluoride (Figure 5).[22] The vinyl groups on the protected hemisphere were intact and the polymer cap was formed by polymerization after removal of the wax. Perro *et al.* reported the synthesis of Janus silica particles on a large scale by modifying the exposed surface of silica particles with amine groups as evidenced by the adsorption with gold nanoparticles on one hemisphere.[23]

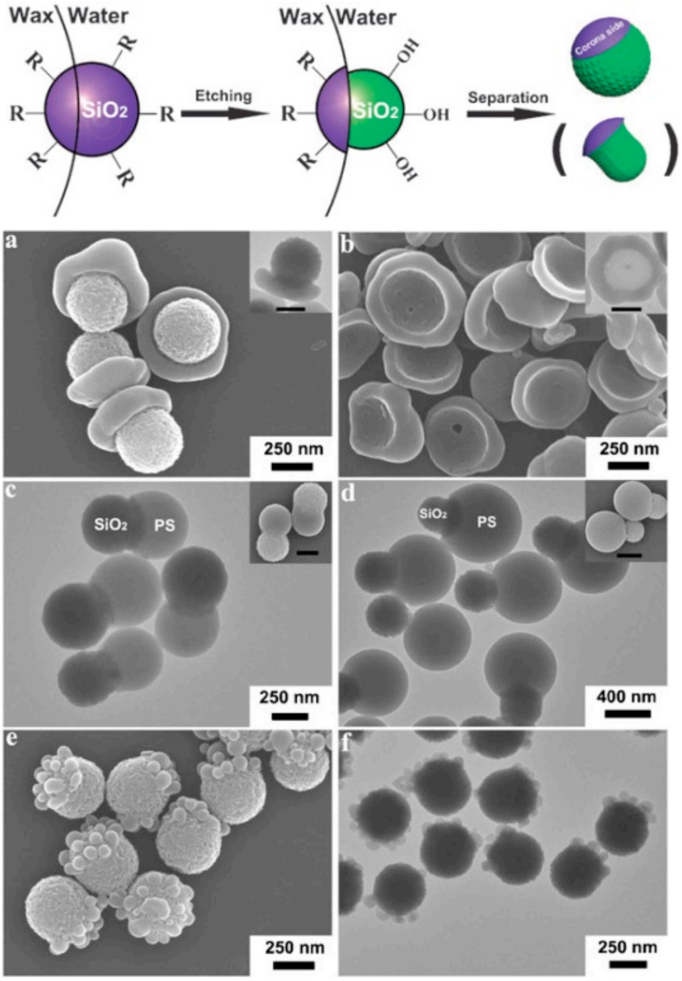

Figure 5. Scheme for synthesis of non-spherical Janus particles by asymmetric wet-etching. SEM and inset TEM microgaphs of (a) Janus SiO_2/PS composite colloids with a PS cap

grown on the corona side; (b) PS nano-caps after removing SiO_2 from (a); (c) - (d) Janus SiO_2/PS dimers with increased PS volume fraction (the dark area corresponding to silica and the grey area corresponding to PS); e) - (f) Janus SiO_2/PS composite colloids with PS nano-flowers grown on the corona side. Reproduced from Ref. [22] with permission from the Royal Society of Chemistry.

He *et al.* prepared Janus $Cu_2(OH)_2CO_3$/CuS microspheres via a Pickering emulsion route by using styrene monomer as the oil phase instead of wax.[24] During the polymerization of styrene, polystyrene microspheres were formed and covered by a layer of $Cu_2(OH)_2CO_3$ particles. The exposed surface was then treated with thioacetamide solution, allowing the conversion of $Cu_2(OH)_2CO_3$ to CuS. The polystyrene core was then removed by treating with toluene at elevated temperature and the Janus $Cu_2(OH)_2CO_3$/CuS microspheres were obtained. Pardhy *et al.* employed both styrene-based and wax-based double Pickering emulsion approach to prepare Laponite clay Janus colloids.[25] In the first step, a Pickering emulsion with styrene as the oil phase was stabilised by Laponite particles. The stable colloids of Laponite-armored polystyrene were then used as solid stabilizers for a second Pickering emulsion with wax as the oil phase. One side of the colloids was trapped in the wax and the exposed side was chemically modified by cation-exchange method, allowing the formation of Janus particle with anisotropic surface charge.[25]

2.1.3. Masking at a liquid-solid interface

In this method, homogeneous particles were immobilized on a solid substrate instead of being trapped at the interface between two fluids. Takei and Shimizu thermally deposited gold onto only one side of latex microspheres facing the evaporation source for subsequent chemical modification with a thiol compound in solution, to form dipolar Janus particles, which could be useful in applications ranging from microscopic probe to biomedicine.[26] One more example of the liquid-solid interface method was reported by Sardar *el al*.[27] Citrate-stabilised gold nanoparticles were immobilized onto a silanized glass surface bearing amine groups by displacing citrate groups. The exposed gold surface was functionalized with a thiol compound bearing hydroxyl group while the masked side of the gold nanoparticles attached to the silane layer was modified with thiols bearing carboxylic or amine group, forming Janus gold nanoparticles as shown in Figure 6. Gold heterodimers were synthesized by the coupling reaction of these asymmetrically functionalized nanoparticles.

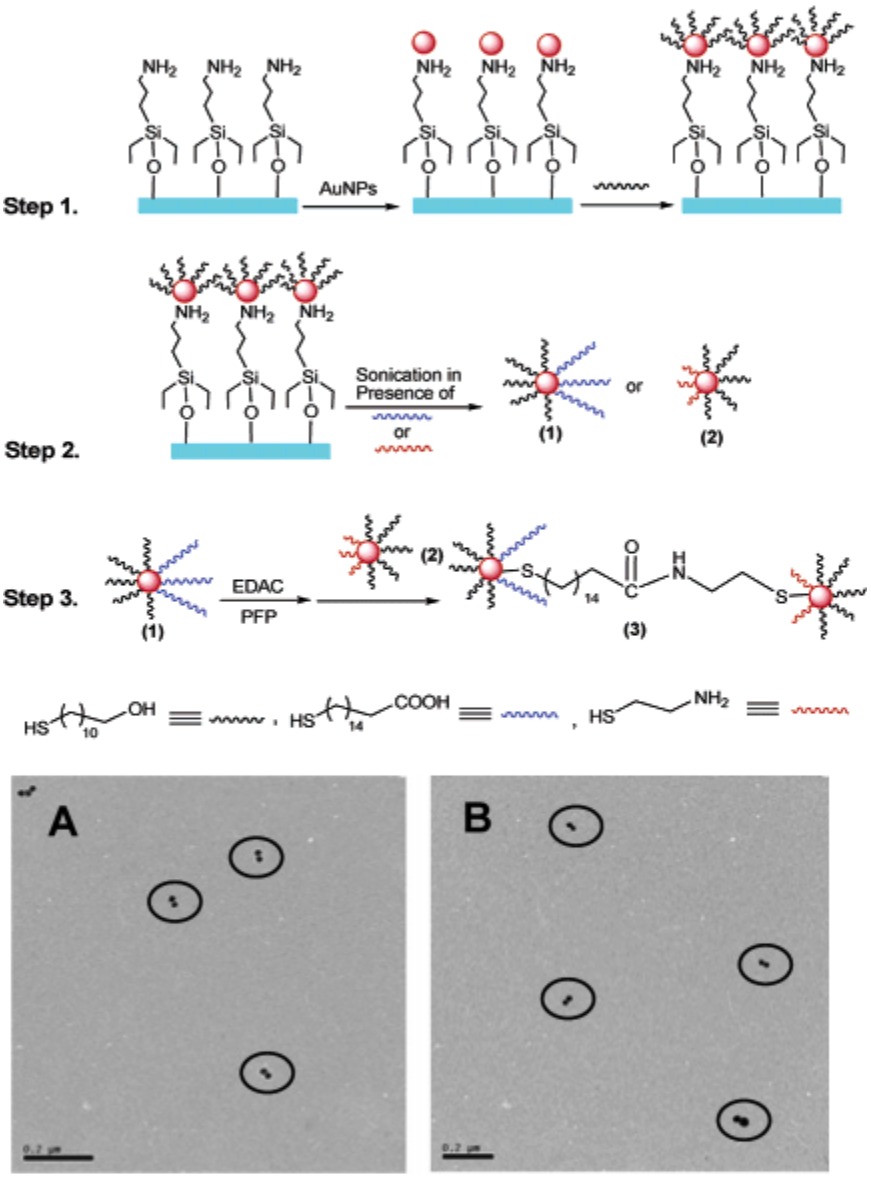

Figure 6. Scheme for the synthesis of gold nanoparticle dimers (top) and TEM images of gold nanoparticle dimers synthesized via coupling of 16-16 nm (A) and 30-30 nm (B) particles (bottom). Scale bar is 200 nm. Reproduced with permission.[27] Copyright (2007) American Chemical Society.

2.1.4. Masking at a gas-liquid interface

A good example for this method is the work of Pradhan *et al.* who prepared Janus gold nanoparticles with hydrophobic character on one side and hydrophilic on the other by using the Langmuir technique (Figure 7).[28] In this study, hydrophobic alkane thiolate-coated gold nanoparticles were dispersed on the water surface at low pressure. Upon mechanical compression, a compact monolayer of hydrophobic gold nanoparticles was formed on the water surface. At high pressure, the interfacial mobility of the nanoparticles was restricted, which favoured the ligand exchange reactions at the particle surface by introducing a hydrophilic thiol ligand such as 3-mercaptopropane-1,2-diol, resulting in the formation of amphiphilic Janus nanoparticles.

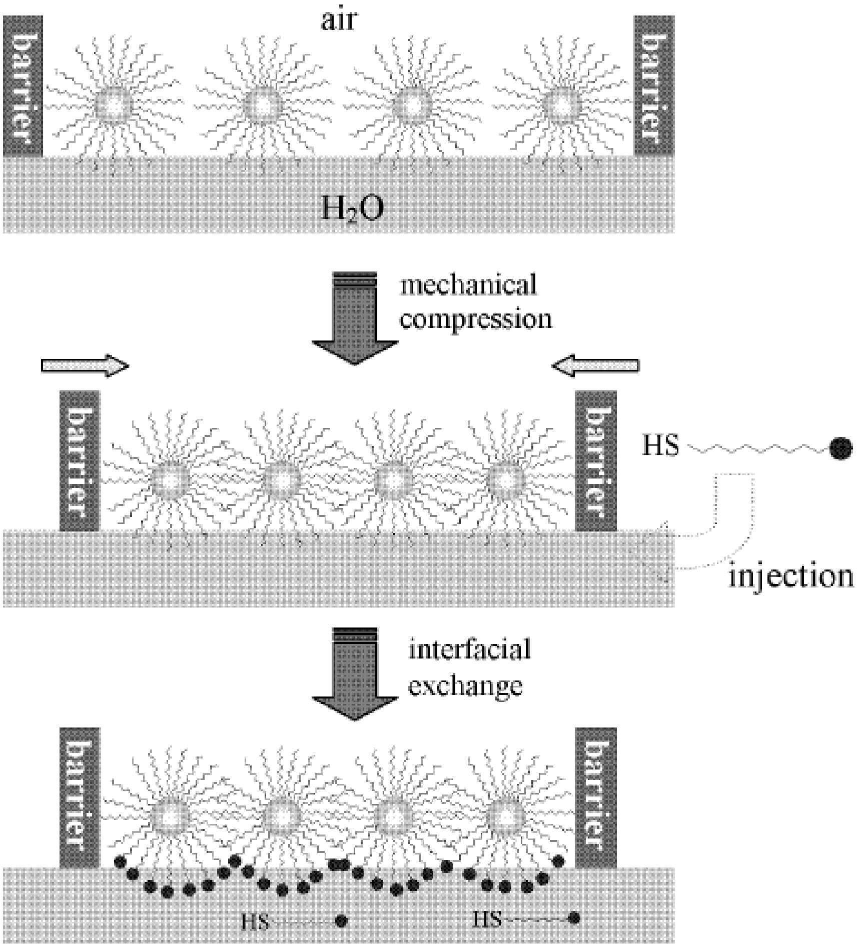

Figure 7. Scheme for preparation of Janus nanoparticles using Langmuir technique. Reproduced by permission of John Wiley & Sons.[28]

2.1.5. Masking at a gas-solid interface

The Whitesides group employed this multi-step gas-solid strategy to prepare hollow metallic hemispheres which could be used as metallic foams, heterogeneous catalysts, magnetic filters, and superhydrophobic surfaces.[29] In the first step, a layer of silica colloids drop-casted on a glass slide was coated with titanium or nickel by electron-beam evaporation. After deposition of a thin film of gold or platinum, metal coated silica particles were detached from the glass slide surface by sonication, followed by treatment with hydrogen fluoride (HF) aqueous solution to dissolve the silica and metallic half-shells were obtained (Figure 8).[29]

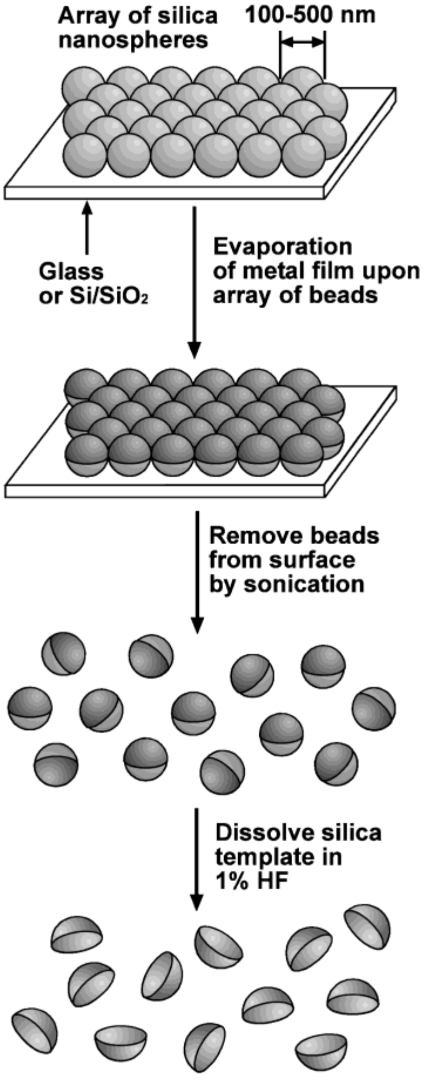

Figure 8. Scheme for fabricating metallic half-shells. Reproduced with permission.[29] Copyright (2002) American Chemical Society.

In summary, although masking is a multi-step process, it is probably one of the most versatile techniques to prepare Janus particles made of different materials with a wide variety of functional groups. There is still a need to improve the method which is even simpler and more accessible for large-scale synthesis of Janus particles.

2.2. Janus micelles by the self-assembly of block copolymers

The self-assembly of amphiphilic block copolymers in solution into symmetric core-shell structures has been studied extensively in the last few decades, since Eisenberg and co-workers in the 1990s discovered the variety of morphologies that can be formed upon microphase separation of two incompatible blocks, including spheres, rods and vesicles.[30] Rapid progress in this attractive research area takes advantage of advanced living/controlled polymerization techniques, which allow the synthesis of block copolymers with well-defined architecture, composition and narrow molecular weight distribution. The preparation of Janus particles through the self-assembly of block copolymers is very challenging and requires extensive study of the thermodynamics of polymer mixtures, as well as the parameters affecting the self-assembly behaviour, such as concentration, temperature, pH, and ionic strength. Different architectures of Janus particles have been prepared by using self-assembly approaches as depicted in Figure 9. This area has been recently reviewed by the Müller group.[3]

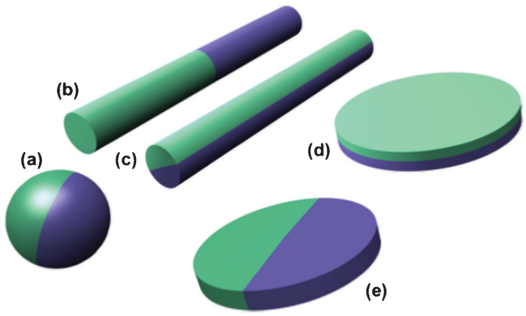

Figure 9. Different Janus particle architectures formed. Architectures (a)–(d) have so far been realized by synthetic and self-assembly approaches for nanoscale polymeric Janus particles. Reproduced with permission.[3] Copyright (2013) American Chemical Society.

Both di-block and tri-block copolymers have been used for the direct synthesis of Janus particles. In the case of diblock copolymers, two combinations can allow for the preparation of Janus micelles. Firstly, a combination of AB and BC diblock copolymers was used for the production of Janus nano-objects, in which the B common segments is insoluble in a given solvent and forms the micellar core.[31-33] Even though sufficient incompatibility of the A and C corona blocks is required for the co-micellization into mixed micelles, a too large incompatibility can lead to the formation of two separate AB and BC micelle populations.[31, 34] Ma *et al.* prepared Janus micelles by co-micellization of PNIPAM-b-P4VP and PEG-b-P4VP in aqueous solutions in the presence of bivalent sulfate ions, which help the crosslinking of positively charged P4VP block.[35] In another approach, Voets *et al.* mixed AB and CD diblock copolymers, poly(acrylic acid)-block-poly(acryl amide) (PAA-b-PAAm) and poly(2-methylvi-nylpyridinium iodide)-block-poly(ethylene oxide) (P2MVP-b-PEO), leading to the forced co-assembly of the two polymers due to electrostatic interactions between the positively charged P2MVP blocks and the negatively charged PAA blocks, while the PEO and PAAm blocks phase-separated on the corona of Janus micelles.[36-39] Wurm *et al.* prepared PEO-b-PPO diblock copolymers bearing a ruthenium end-group via ring opening polymerization and observed the formation of Janus micelles and their assembly into higher ordered super-micelles.[40]

In the case of ABC triblock terpolymers, Janus micelles could be assembled with two outer soluble end-blocks, A and C, and an inner insoluble block, B. The Müller group pioneered the synthesis of Janus particles based on the self-assembly of triblock copolymers with central polybutadiene block able to crosslink, as depicted in Figure 10.[2-3, 41] The structures of Janus micelles formed within thin films were well-ordered, and consisted of a cross-linked core and a corona with two different hemispheres. This method was explored extensively by the same group and Janus morphologies such as spheres,[41] cylinders,[42] discs[43] and lamellae[44] were observed depending on the nature of terpolymers and relative length of blocks. The key for successful Janus particle synthesis is the use of polybutadiene allowing the crosslinking reaction after film casting of the terpolymer. Janus particles with different morphologies were obtained upon dissolution of the film with suitable solvent and sonication. The self-assembly of triblock copolymer in solution was also employed by other groups for the preparation of Janus particles. Sfika *et al.* prepared pH-responsive Janus star-like micelles from double hydrophilic poly(2-vinylpyridineb-poly(methyl methacrylate)-b-(poly(acrylic acid) (P2VP-PMMA-PAA) terpolymer in aqueous dilute solutions.[45] Du and Armes reported the formation of Janus particles by dissolving directly a primary amine-based triblock copolymer, poly(ethylene oxide)-b-poly(3-caprolactone)-b-poly(2-aminoethyl methacrylate) (PEO-b-PCL-b-PAMA) in water, with PCL phase separating in the core and the two hydrophilic PEO and PAMA blocks on the surface. The PCL core was selectively modified with tetramethyl orthosilicate leading to the formation of Janus nanostructures with a silica core within a PAMA-rich hemisphere.[46]

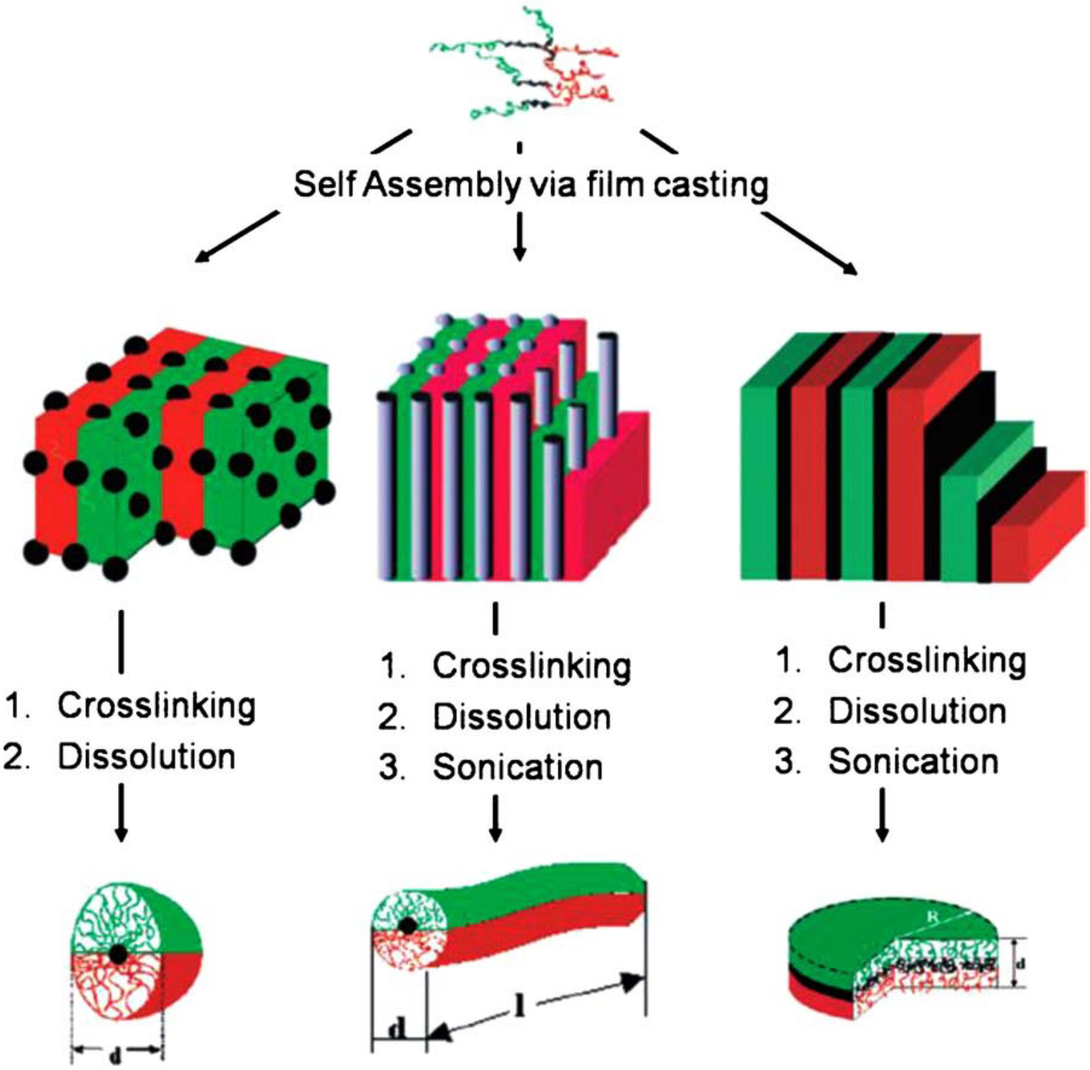

Figure 10. Scheme for the preparation of Janus nanoparticles from terpolymers. The process starts with film casting of the terpolymer, followed by cross-linking of the intermediate block and finally by dissolution and sonication. Depending upon the structure and molecular weight of the terpolymer, film casting produces matrices with different morphologies: spherical, cylindrical and disk-like. Reproduced from Ref. [2] with permission from the Royal Society of Chemistry.

2.3. Synthesis of Janus nanoparticles from phase separation method

In this method, the incompatibility of two polymers in a confined environment induces a powerful driving force for the phase separation of polymer mixtures, resulting in the formation of Janus structures. Janus nanoparticles of two inorganic, two organic or hybrid lobes can be prepared using the phase separation method as described in recent reviews.[4-5] This Section will provide more detailed descriptions about Janus nanoparticles synthesis using seeded emulsion polymerization method. Among the synthetic approaches for Janus nanoparticles, emulsion based method is the most effective method on a large scale. The seeded emulsion polymerization method starts with preformed solid seed particles dispersed in emulsions, followed by the swelling with additional monomer. The preformed seeds can be crosslinked or uncrosslinked. Subsequent polymerization can induce the phase separation to obtain non-spherical Janus nanoparticles with two chemically distinct parts.

2.3.1. Formation of Janus nanoparticles from crosslinking seeds

Seeded polymerization which has been described by Sheu *et al.* is one of the most flexible methods to prepare Janus particles with easy scalability. [9] This method involves the swelling of preformed cross-linked seed particles with monomer that during polymerisation is expelled from the core to form a bulge in the Janus particles. It is a prerequisite that the swollen monomer and the seed matrix are incompatible, resulting in the phase separation of the newly formed polymer from the seed particles. In addition, the use of crosslinking agent is important for the monomer to be expelled onto the surface of the seed particles due to the high internal stress, especially at elevated temperature, which induces the formation of the Janus structure after free radical polymerization. The morphology of the anisotropic particle is governed by many different parameters including the degree of crosslinking of the seeds, the hydrophilicity of seed surface, the wettability of the monomer, size of the seeds and monomer/polymer swelling ratio.[6, 9, 47]. Formation of these particles followed the same mechanism discussed by Mock *et al.*[6] and Pham *et al.*[8] and presented in Figure 11, where crosslinked polymer networks of the monomer-swollen seed particles shrunk on heating, expelling the polymerizing monomers. Depending on the wettability of the expelled monomers on the seed particles, different particle morphologies were formed. The wetting of the surface by the monomer was in turn influenced by stabilizing groups on the seed particle surface and compatibility between the extruded monomers and the seed polymer. Polymerization of the protruded monomers produced distinct bulges attached to the original seed particles

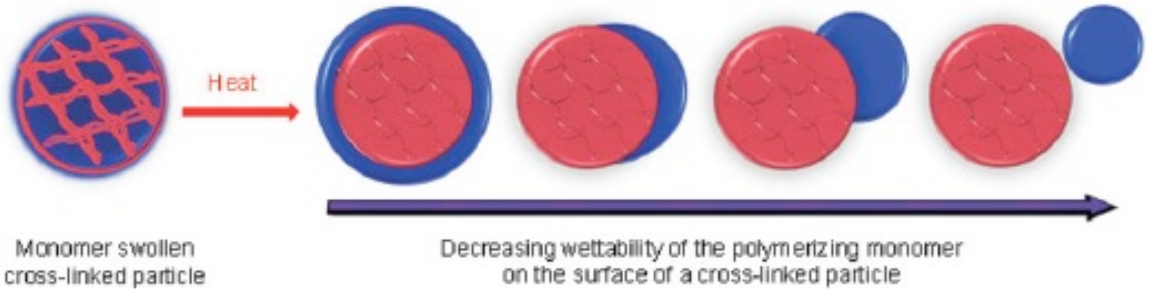

Figure 11. Schematic behaviour of the monomer swollen cross-linked polymer seed on heating. The wetting ability of the monomer governs the morphology of the anisotropic particles formed during subsequent polymerization. In the reactions described here, complete detachment of a new particle is prevented by RAFT control making the new polymer continuous with the old. Reproduced from Ref. [8] with permission from the Royal Society of Chemistry.

The Weitz group prepared uniform Janus particles with chemical anisotropy in the micrometer range based on this technique, using crosslinked polystyrene seeds swollen with methyl methacrylate and butyl methacrylate which are immiscible with polystyrene.[48] This group also reported the synthesis of amphiphilic dumbbell Janus particles consisting of one hydrophilic poly (ethylene imine)-coated polystyrene lobe and one hydrophobic polystyrene lobe by employing surface modification. Interestingly, different shapes of anisotropic particles could be formed, including rod, cone, triangle, and diamond, depending on the crosslinking density gradients between the lobes.[49] This versatile strategy was employed by

Tang *et al.* to prepare Janus polyacrylonitrile (PAN)/polystyrene (PS) polymer colloids particles via styrene polymerization onto crosslinked PAN hollow spherical seeds.[14] Subsequent hydrolysis of PAN on one lobe leads to the formation of functional carboxylic acid, enabling a selective functionalization with magnetite and silica, as illustrated in Figure 12. The prepared inorganic/organic composite Janus colloids can be used as solid surfactants.

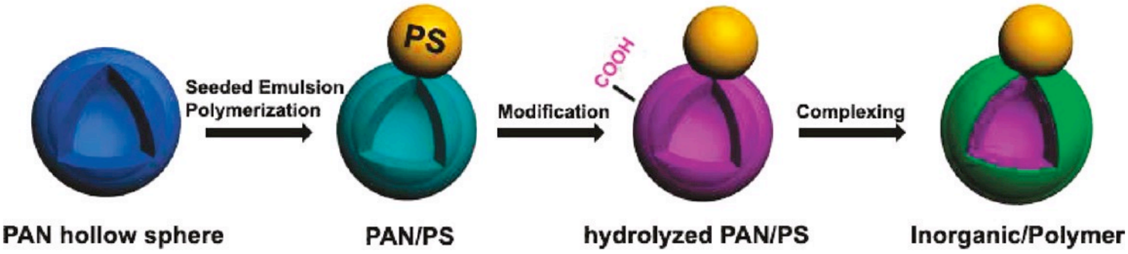

Figure 12. Schematic synthesis of mixed polymer/inorganic Janus colloids. Reproduced with permission.[14] Copyright (2010) American Chemical Society.

By using the same immiscible pairs PS/PAN, Huang *et al.* synthesized raspberry-like PS–polyacrylonitrile (PAN) particles with multiple protrusions of PAN on the PS surface.[50] During the polymerization of AN monomer by γ-ray radiation, PAN polymer chains segregated from the crosslinked styrene-divinylbenzene-acrylic acid terpolymer (P(S-DVB-AA)) seed particles and multiple PAN lobes were formed onto the surface of the seeds due to the insolubility of AN monomer and PAN polymer (Figure 13).[50]

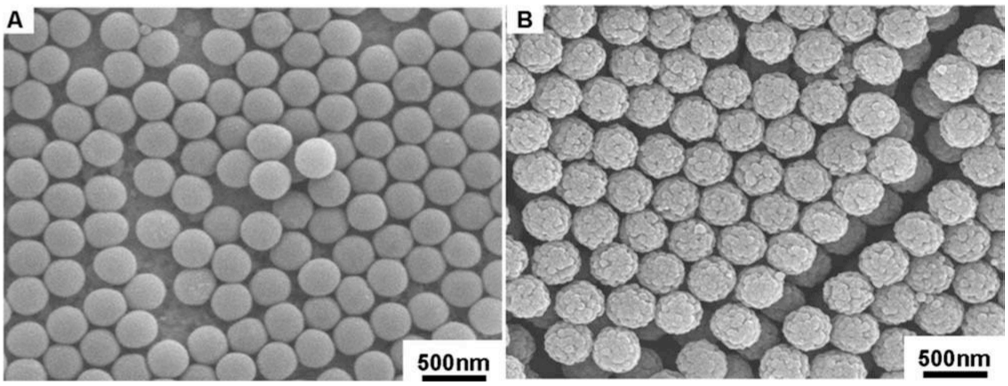

Figure 13. FESEM micrographs of (a) P(S-DVB-AA) particles and (b)PS/PAN raspberry-like particles. Reproduced by permission of John Wiley & Sons.[50]

In another study, the appearance of protrusions of polystyrene onto highly cross-linked poly(N-isopropylacrylamide) (polyNIPAM), polystyrene, and magnetite filled polyNIPAM as seed particles could be varied by varying the surfactant concentration, resulting in particles with multiple lobe particles. The roughness could be tuned by varying the experimental conditions such as initiator, surfactant, styrene concentrations and also polymerization temperature (Figure 14).[51]

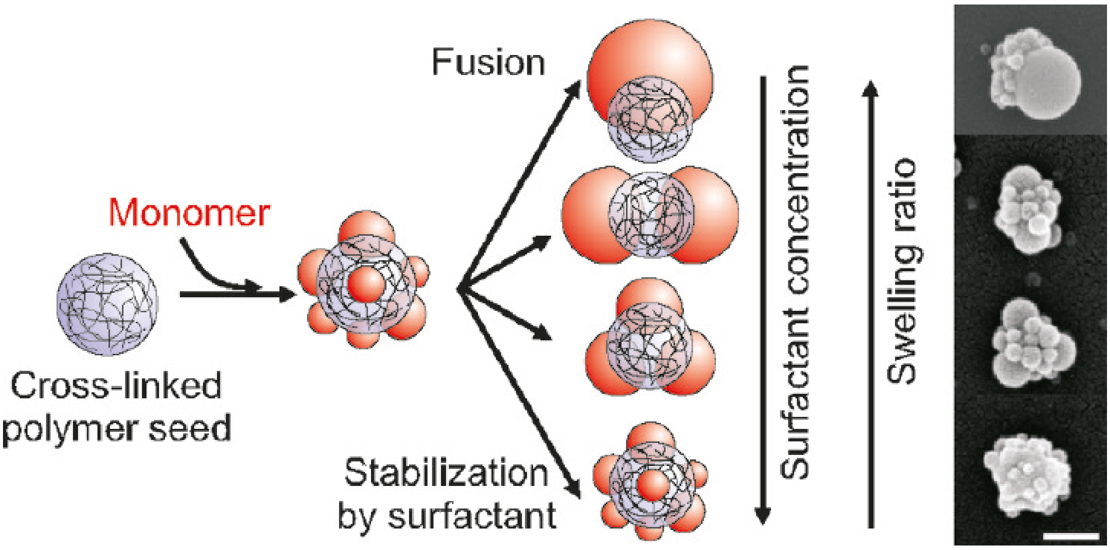

Figure 14. Schematic of the synthesis of multiple lobe particles, with systematic variation of several factors on the resulting patchy particles. Reproduced with permission.[51] Copyright (2011) American Chemical Society.

The Okubo group employed a different approach for the preparation of spherical and "snowman-like" hydrophobic Janus particles by the solvent evaporation method.[52-53] Atom transfer radical polymerization (ATRP) was employed in combination with solvent evaporation method by this group as an elegant approach to prepare amphiphilic mushroom-like Janus particles in a two-step synthetic methodology. As shown in Figure 15, in the first step spherical poly(methyl methacrylate) (PMMA)/poly(styrene-2-(2-bromoisobutyryloxy)ethyl methacrylate) (P(S-BIEM)) macroinitiator Janus particles were formed, due to the phase separation induced by solvent evaporation. Subsequently, 2-(dimethylamino)ethyl methacrylate (DM) monomer was further polymerized via surface-initiated ATRP mechanism to form pH-responsive mushroom-like PMMA/P(S-BIEM)-graft-poly(DM).[54] The prepared mushroom-like Janus particles with amphiphilic character could be used as solid surfactants to stabilize oil-in-water emulsion. The stability of the emulsion was controlled by changing pH and temperature, which could lead to the adsorption/desorption of the stimuli-responsive Janus particles.[55]

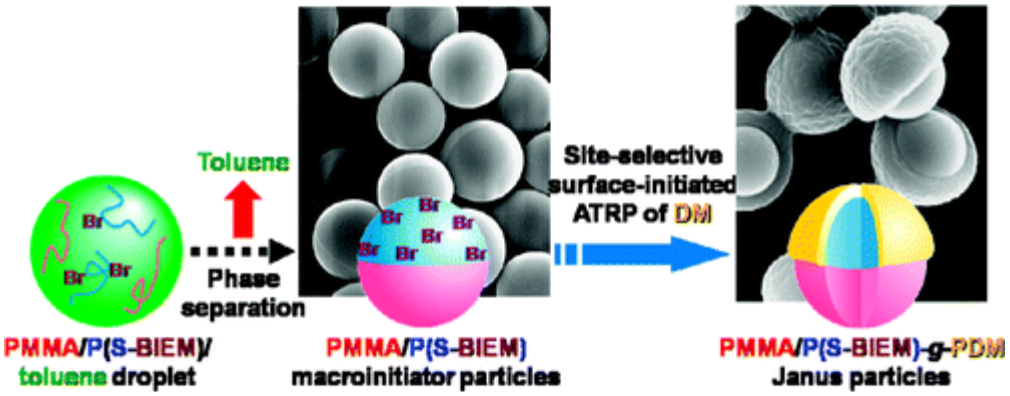

Figure 15. Preparation of "mushroom-like" Janus particles by site-selective surface-initiated atom transfer radical polymerization in aqueous dispersed systems. Reproduced with permission.[54] Copyright (2010) American Chemical Society.

Our group recently reported the synthesis of polymeric Janus nanoparticles based on this seeded emulsion approach using Reversible Addition Fragmentation chain Transfer (RAFT) polymerization.[8] We pioneered the use of RAFT to mediate the emulsion polymerization processes.[56-57] The synthesis of polymer Janus nanoparticles in this work consists of five steps, as described in Figure 16. In what follows, the synthesis will be described in more detail.

Amphiphilic diblock copolymers containing hydrophobic block of polystyrene and hydrophilic block of poly(acrylic acid) or poly(acrylamide) were first synthesized using RAFT polymerization as shown in Figure 17. The prepared diblock copolymers were self-assembled into micelles in water with an average size of 20 nm after neutralization of the carboxylic acid functional groups (step 1). The formed micelles were swollen by monomer, which then underwent further free radical emulsion polymerization to chain extend the hydrophobic polystyrene blocks. At this stage, the initial micelles were "locked in" to nanoparticles stabilized by the negative charges of polyacrylic acid or steric hydrophilic hairy layers of polyacrylamide blocks (step 2). The nanoparticles were then crosslinked by divinyl benzene to generate uniform spherical crosslinked seeds (step 3). Seed nanoparticles were swollen with monomers such as styrene or methyl methacrylate/butyl acrylate mixture, by simply mixing the monomers and particles overnight under constant stirring (step 4). Polymeric Janus nanoparticles which are anisotropic in shape, chemical composition and surface property were obtained after polymerizing monomer swollen cross-linked seed particles (step 5). It is interesting that the shape of Janus nanoparticles was controlled by varying the charge density of the initiator and the composition of monomer swollen in the crosslinked seeds. While Janus ellipsoidal nanoparticles were formed when V-501 was used as an initiator to grow the cross-linked seed particles, snowman shaped anisotropic particles were obtained when KPS was used (Figure 18A, B and C). When styrene was replaced by a blend of MMA/BA monomers, we observed the formation of dumbbell shape. (Figure 18D). The preparation of Janus particles by growing newly formed polymer onto the surface of preformed seeds involves several steps. An approach which can produce anisotropic particles directly is highly sought after.

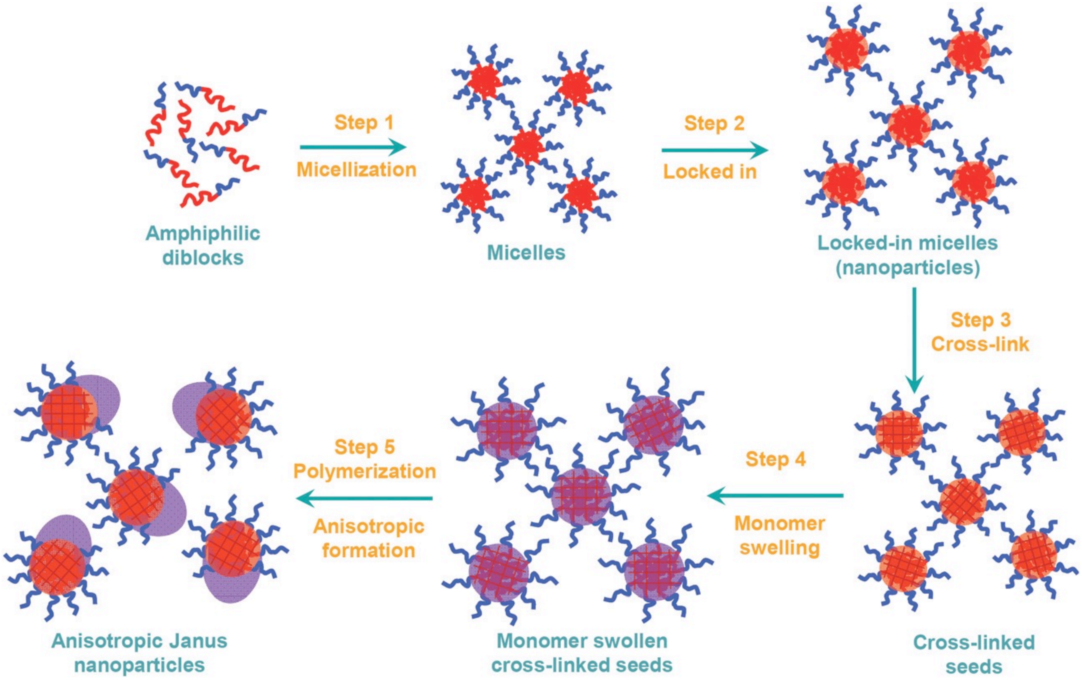

Figure 16. Schematic procedure for the synthesis of anisotropic Janus nanoparticles. Reproduced from Ref. [8] with permission from the Royal Society of Chemistry.

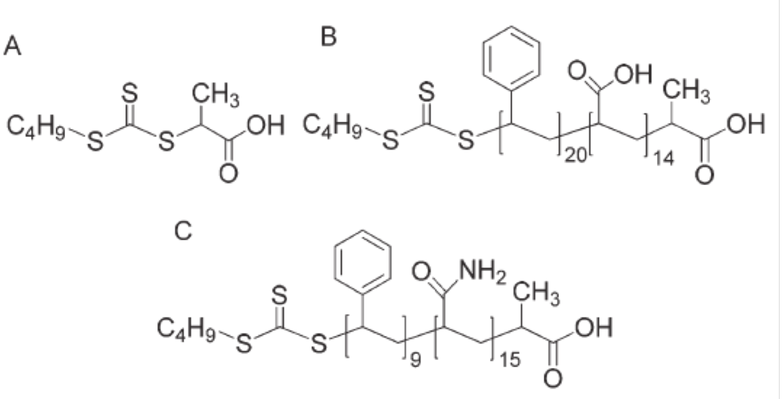

Figure 17. Structure of RAFT agent (A) and RAFT diblock of styrene and acrylic acid (B) or styrene acrylamide (C). Reproduced from Ref. [8] with permission from the Royal Society of Chemistry.

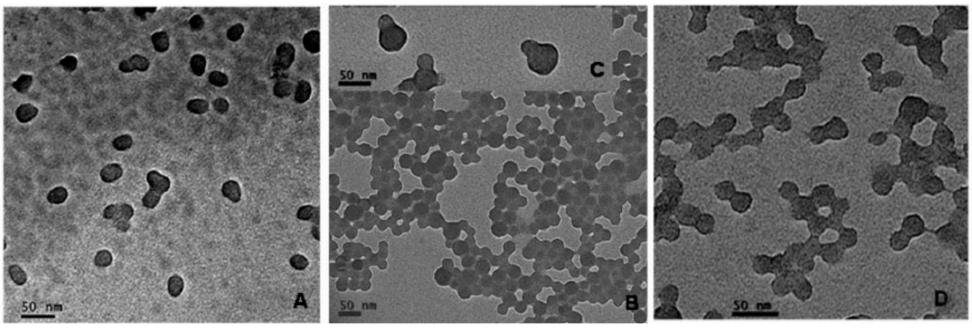

Figure 18. TEM micrographs: (A) ellipsoidal; (B,C) snowman shaped; (D) dumbbell shaped polymer Janus nanoparticles. Reproduced from Ref. [8] with permission from the Royal Society of Chemistry.

In addition to polymeric Janus particles, polymer-inorganic hybrid particles were extensively studied. Ge *et al.* described the synthesis of asymmetric composite colloids consisting of two lobes: one lobe contains shell-crosslinked Fe_3O_4@SiO2@PS composite colloids (Figure 19B) and the other containing polystyrene phase-separated after polymerization of swollen styrene at elevated temperature (Figure 19 C and D).[58] These uniform and well-defined anisotropic structures could be useful for novel devices and materials.

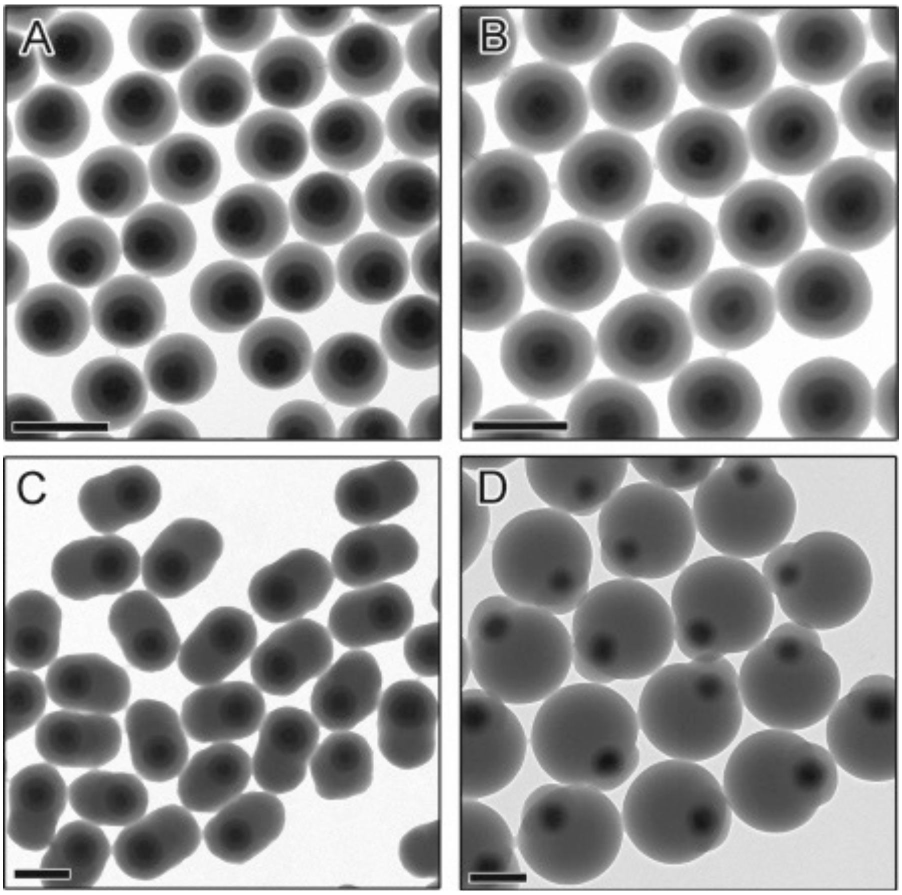

Figure 19. TEM micrographs of a series of Fe3O4@SiO2@PS composite colloids with complex structure produced by emulsion polymerization of styrene using MPS grafted Fe3O4/SiO2 particles as seeds: (A, B) Spherical colloids produced in one-step emulsion polymerization (A) without, and (B) with DVB as crosslinker; (C) Ellipsoids formed by swelling and phase separation in one-step emulsion polymerization; (D) Doublets produced by separated steps of swelling and phase separation. All scale bars are 400 nm. Reproduced with permission.[58] Copyright (2007) American Chemical Society.

2.3.2. Formation of Janus nanoparticles without crosslinking seed

From the previous Section, it is very common for the synthesis of Janus particles by seeded polymerization method that the seeds are crosslinked with difunctional reactive monomers such as divinylbenzene (DVB) which facilitates the polymer protrusion, resulting in the formation of anisotropic structures.[47]

In another approach, Nagao *et al.* reported the successful synthesis of anisotropic polymer particles using surfactant free emulsion polymerization in the presence of the reactive silane coupling agent 3-methacryloxypropyltrimethoxysilane (MPTMS) instead of difunctional DVB monomer (Figure 20).[59] This method allows the preparation of anisotropic polymer particles containing inorganic particles, such as silica, which can be removed by dissolving in hydrofluoric acid to form hollow polymer particles.

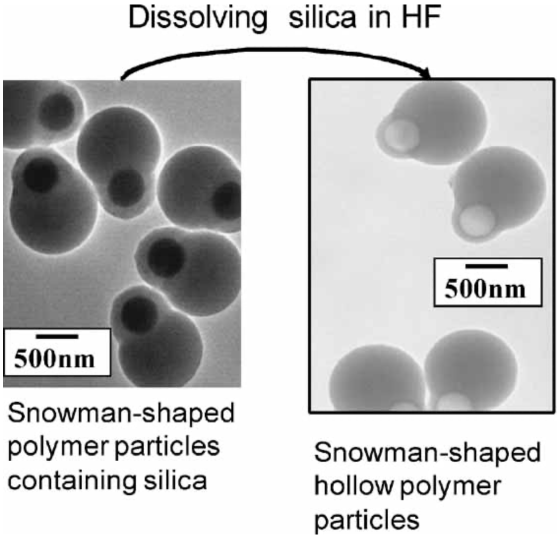

Figure 20. Synthesis of anisotropic polymer particles with soap-free emulsion polymerization in the presence of a reactive silane coupling agent. Reproduced by permission of John Wiley & Sons.[59]

Janus hybrid colloidal particles with various metal nanoparticles including Au and Ag were synthesized by Xia *et al.* using a simple, robust and scalable approach.[60] The key for the successful synthesis of uniform metal-PS asymmetric particles with only one metal nanoparticle on its surface is the addition time point for metal nanoparticle colloids which is only few minutes after the polymerization process (Figure 21). The addition of metal nanoparticles prior the polymerization can lead to the formation of PS beads which contain aggregates of metal nanoparticles instead of one single nanoparticle. The yield of hybrid particles is only 50% when metal nanoparticles were added 30 min after polymerization. This is a robust strategy for the synthesis of hybrid Janus particles. Even though the type of metal particles and their size should not influence the yield, the amount of added styrene monomer was found to be crucial for achieving 100%.

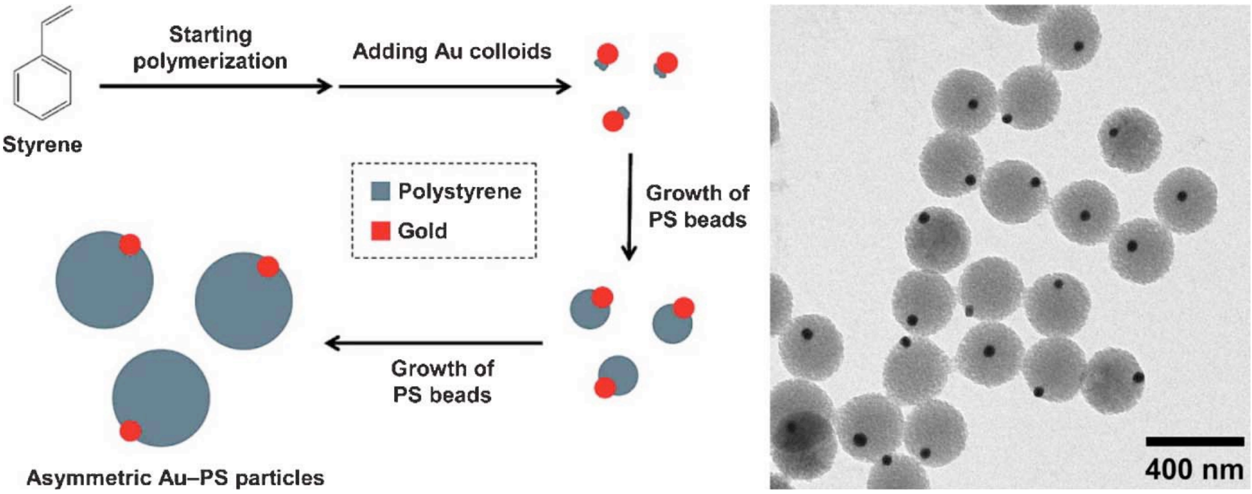

Figure 21. Schematic diagram for the synthesis of asymmetric Au–PS Janus nanoparticles and their morphology. Reproduced with permission.[60] Copyright (2009) American Chemical Society.

Yu *et al.* reported an alternative strategy to produce anisotropic polymer particles with a snowman-like shape with two distinct lobes in few minutes by the protrusion of un-crosslinked polystyrene core from a polyelectrolyte multilayer shell in a water and tetrahydrofuran (THF) mixture (Figure 22).[61] It was crucial to use mixed solvents to prevent the complete dissociation of polystyrene in THF, resulting in the formation of a polyelectrolyte multilayer capsule. The process could be extended to different materials to generate both Janus particles with both structural and chemical contrast.

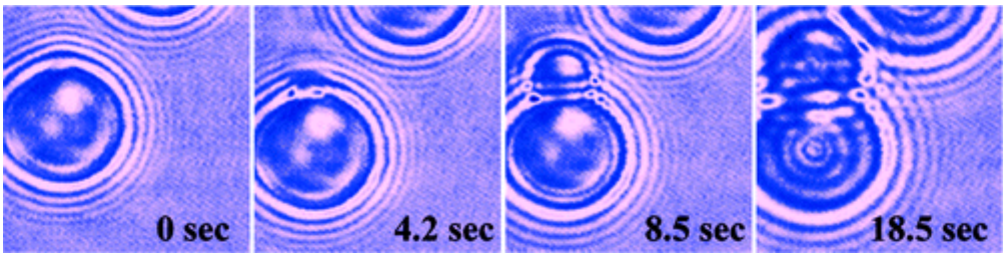

Figure 22. Genesis of anisotropic colloidal particles via protrusion of polystyrene from polyelectrolyte multilayer encapsulation. Reproduced with permission.[61] Copyright (2009) American Chemical Society.

In a similar approach, Park *et al.* found that dumbbell-shaped nanoparticles could easily be synthesized by emulsion polymerization without cross-linking of seed particles. When PS–poly(St-cotrimethoxysilylpropylacrylate (TMSPA)) core–shell particles were swollen with a monomer, the hydrophobic PS core was expelled onto the hydrophilic shell, forming another lobe of dumbbell-shaped polymer Janus particles (Figure 23).[62]

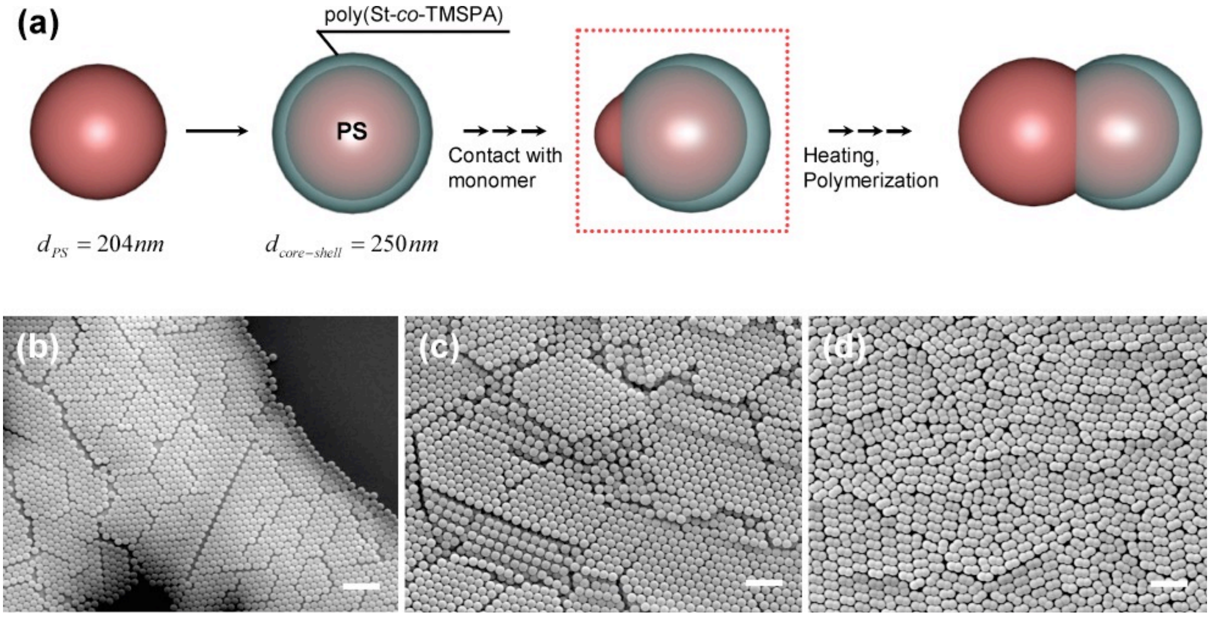

Figure 23. Synthesis of dumbbell-shaped polymer nanoparticles: (a) Schematic representation of two-step seeded emulsion polymerization. (b-d) Scanning electron micrographs of (b) PS nanoparticles, (c) PS/poly(St-co-TMSPA) core-shell nanoparticles, and (d) symmetric

dumbbell-shaped. Reproduced with permission.[62] Copyright (2010) American Chemical Society.

In summary, among the approaches for the synthesis of Janus nanoparticles, seeded emulsion based method is the most efficient and promising in scalability, cost effectiveness and varied composition, relevant to industrial application. The composition of Janus nanoparticles can be easily controllable by post modification of each compartment with functional groups.

3. Properties of Janus nanoparticles

Recent advancement in nanotechnology enabled the synthesis of Janus particles with various shapes other than just spherical, including ellipsoids, dumbbells and snowman. Due to their asymmetric structure and chemical composition, Janus nanoparticles possess a number of unique properties compared with their homogeneous counterparts. Janus nanoparticles may have one lobe composed of hydrophilic groups and the other hydrophobic groups[63] which gives Janus particles unique properties of both surface activity and amphiphilicity, compared to homogenous particles which can only present surface activity.[64] Surface activity relates to the tendency to adsorb at interfaces, while amphiphilicity implies the two parts have different affinities for different chemical environments.

3.1 Interaction of amphiphilic Janus particles at interfaces

Based on theoretical prediction, Binks and co-workers showed amphiphilic Janus nanoparticles adsorb at the water-oil interfaces with three times stronger energy than homogenous nanoparticles with the same size and chemical nature.[64-65] Experimental data qualitatively confirmed Binks' theoretical prediction of the effect of Janus particles at liquid-liquid interfaces. The stronger attachment of Janus nanoparticles at the water-oil interface can be attributed to their amphiphilic properties as interfacial activity was increased by increasing the amphiphilic character of the particles (Figure 24). [66] This property of Janus nanoparticles makes them more advantageous in the stabilization of emulsions than homogeneous analogs.[67]

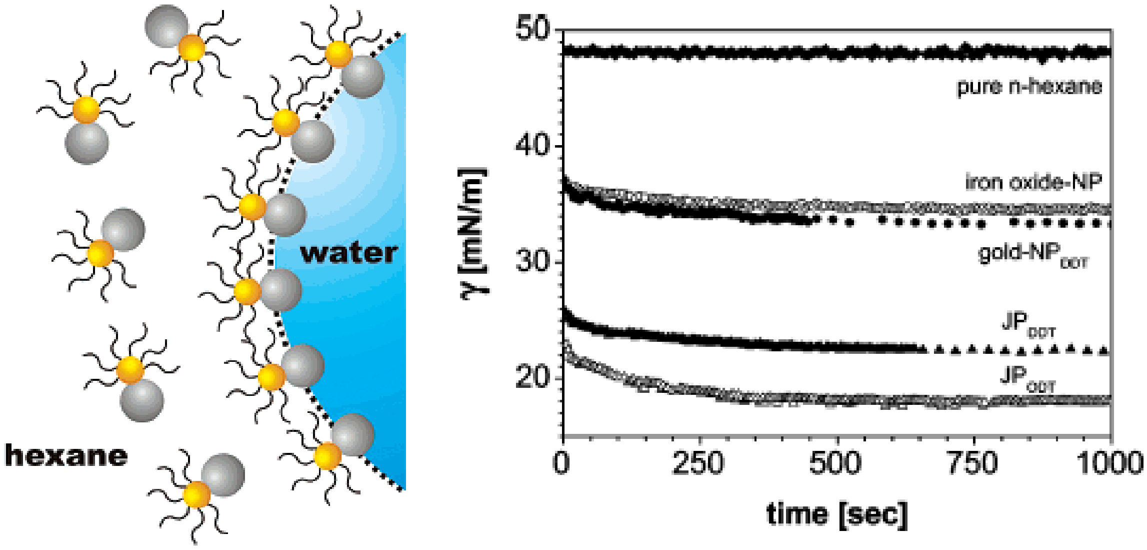

Figure 24. Schematic representation of Janus particles at the hexane/water interface (left) (yellow: gold part; gray: iron oxide part) and interfacial tension vs time (right). NP: homogeneous nanoparticles, JP: Janus particles. The gold parts were modified using dodecanethiol (DDT) or octadecanethiol (ODT). Reproduced with permission.[66] Copyright (2006) American Chemical Society.

It is noted that the geometry of Janus particles influence strongly on their surface activity.[68-70] Bon and co-workers studied the interfacial tension of Janus spheres, Janus cylinders, and Janus discs based on both experimental and simulation data. Interfacial activity of the Janus particles measured by pendant drop technique due to their adsorption at an oil-water interface was strongly influenced by Janus particle shape (Figure 25). Janus cylinders showed the maximum reduction in the equilibrium interfacial tension. Janus spheres showed a moderate reduction in surface activity. The addition of Janus discs resulted in the smallest reduction in interfacial tension. Simulation and experimental data also showed the change in Janus nanoparticle shape from sphere to cylinder and disc influenced not only the interfacial tension but also adsorption kinetics, packing behavior, and energy barriers.[70]

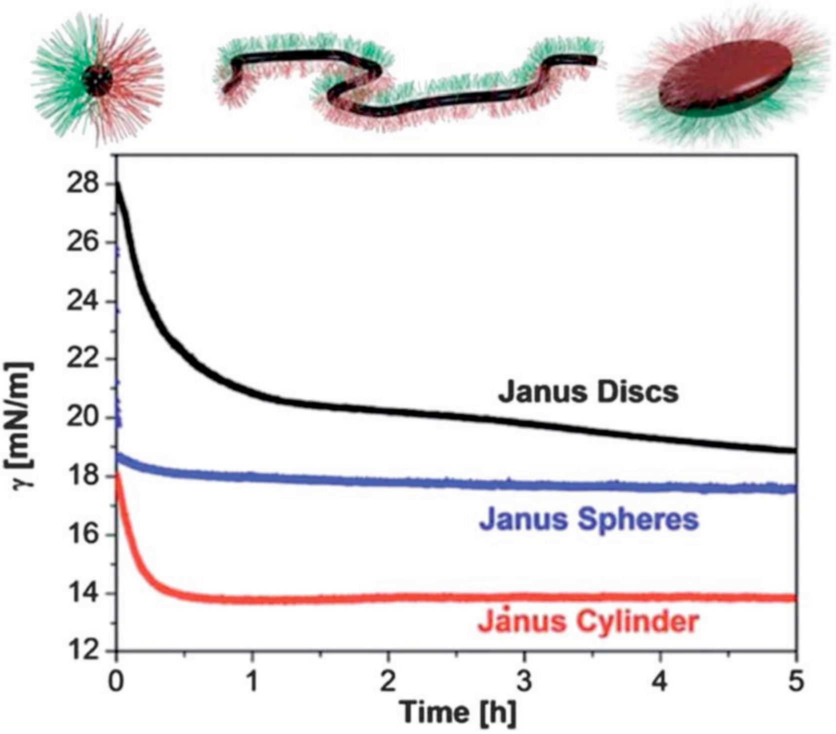

Figure 25. Influence of the Janus particle shape on the interfacial tension at a water/toluene interface. Reproduced with permission.[70] Copyright (2013) American Chemical Society.

3.2. Self-assembly

Janus particles have the ability to self-assemble into complex hierarchical structures in both aqueous and organic solvents.[41, 43, 69, 71-76] For example, spherical Janus micelles having one half of polystyrene (PS) and other half of poly(methyl methacrylate) (PMMA) self-assemble into clusters in various organic solvents, such as tetrahydrofuran.[41] The Müller group observed the controlled self-assembly of their prepared Janus amphiphilic micelles into supramicelles with different shapes including cylinders,[42, 77] spherical[2] and disks[43-44] in water, with the PS side facing each other and the PMAA side exposed to the water above a critical concentration.[3]

He *et al.* described a novel strategy for the synthesis of silica Janus particles with controlled asymmetric shapes including moon-like, dumbbell and rod-like.[78] The surface of both lobes of the prepared Janus particles can be chemically modified to introduce amphiphilic features, allowing the spontaneous self-arrangement into various clusters such as hollow spherical or tube-like morphology (Figure 26). These dense structures could be useful for a wide range of applications such as self-assembly, photonic crystals, and drug delivery.

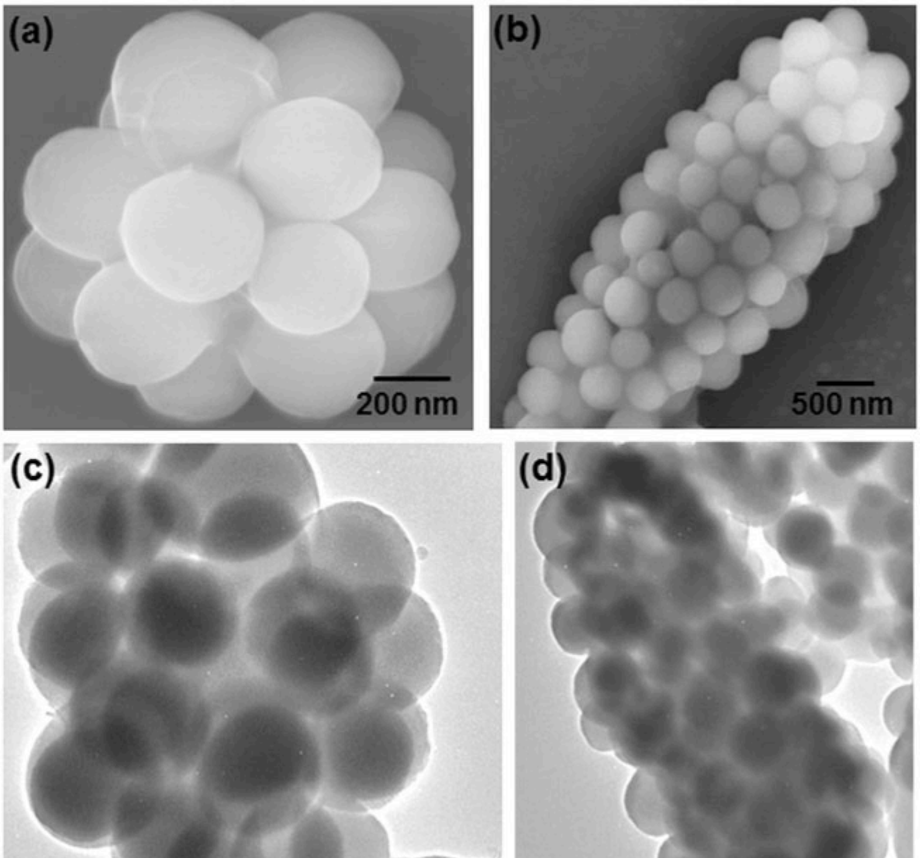

Figure 26. Self-assembly of amphiphilic Janus particles in water–ethanol (1 : 1, vol) mixture. SEM and TEM micrographs of (a, c) hollow clusters; (b, d) tube-like self-assembled structures. Reproduced from Ref. [78] with permission from the Royal Society of Chemistry.

Hong *et al.* studied the assembly of spherical particles with opposite electric charge, ‘zwitterionic’ micron-sized Janus particles. The shapes of self-assembled clusters was characterized by epifluorescence microscopy and Monte Carlo computer simulations, which showed that charge asymmetry of individual Janus particles is preserved in the clusters.[74]

The self-assembly of Janus particles can also be controlled by various parameters including pH, temperature and external field. The Hatton group studied extensively the self-assembly behaviour of prepared Janus particles composed of magnetite nanoparticles coated on one lobe with poly(acrylic acid) (a pH-dependent polymer) and functionalized on the other lobe with either polystyrene sodium sulfonate (a pH-independent polymer) or poly(N-isopropyl acrylamide) (temperature-dependent polymer) (Figure 27). It was found that their prepared Janus nanoparticles are monodispersed at high pH values and low temperatures, but can self-assemble at pH values less than 4 (for PSSNa) or at high temperatures than 31 °C (for PNIPAM) to form stable dispersions of clusters of approximately 80-100 nm in size.[79-80]

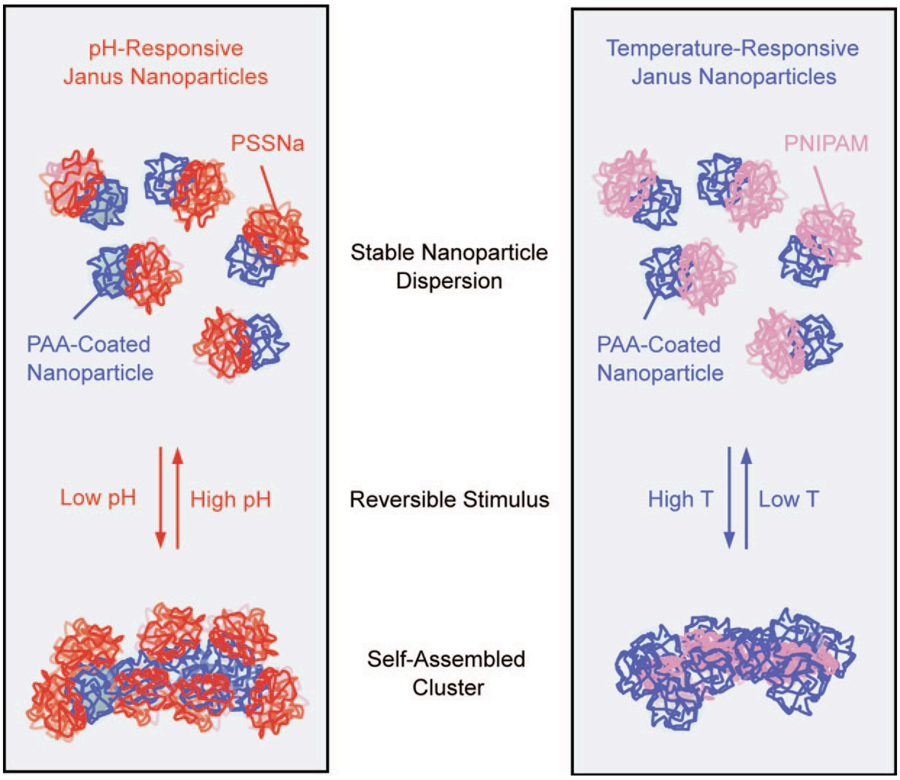

Figure 27. Schematic representation of the Janus nanoparticles and their self-assembled structures on application of an appropriate stimulus. Note that the PSSNa polymers constitute

the stabilizing shell of the clusters, while the PNIPAM chains collapse and form the hydrophobic core of the clusters. Reproduced with permission.[80] Copyright (2008) American Chemical Society.

The formation of chain-like assemblies of aforementioned concentric and eccentric Janus magnetic nanoparticles was observed when they were subjected to a magnetic field (Figure 28).[58] The morphology of the chain was linear for concentric particles, whereas zigzag chains were observed for eccentric ones. This observation was in good agreement with another magnetic Janus particle system.[81]

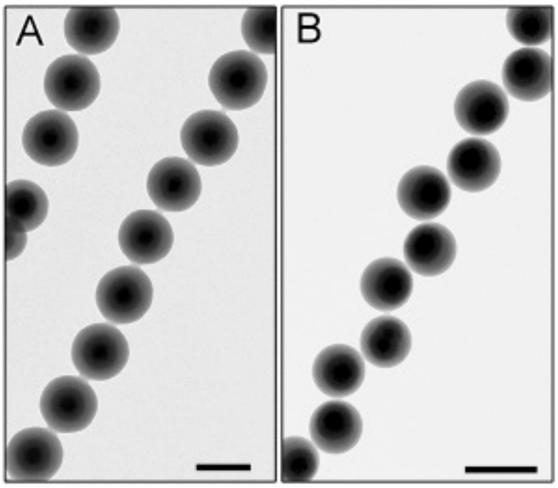

Figure 28. TEM micrographs of self-assembled chainlike structures of (A) concentric and (B) eccentric spherical colloids under an external magnetic field. Both scale bars are 400 nm. Reproduced with permission.[58] Copyright (2007) American Chemical Society.

4. Applications of Janus nanoparticles

Janus particles possess unique properties which make them "smart" materials in a wide range of applications including stabilizers for emulsion[82], catalyst in hydrogen peroxide decomposition[83], water-repellent fibers[84], biomolecular sensing[85], imaging and magnetolytic therapy[86-87], elctrotrics[88] and drug delivery[5]. In this Section, we will showcase the use of Janus nanoparticles in emulsion stabilization and drug delivery.

4.1 Emulsion stabilization

The chemical asymmetry of Janus particles can introduce amphiphilic properties that induce the particles to self-assemble,[74, 89] and allows them to be used to stabilise oil/water emulsions.[11, 66, 70] Emulsions stabilised by Janus particles are more stable than those prepared with homogeneous particles, because the higher adsorption energy of a Janus spherical particle to a fluid-fluid interface.[64, 90] Due to the difference in hydrophobicity between the seed and the bulge, the Janus nanoparticles synthesized by us using seeded emulsion polymerization approach showed good surface activity. We demonstrated the formation of polymer particles stabilized by ellipsoidal polystyrene Janus particles in a surfactant-free ab-initio free radical emulsion polymerization of styrene or BA/MMA.**[8]** The Janus NPs appear to play an important role in the nucleation and stabilization of the particles formed in an ab-initio surfactant free emulsion polymerization as well as particle size distribution as shown in Figure 29.

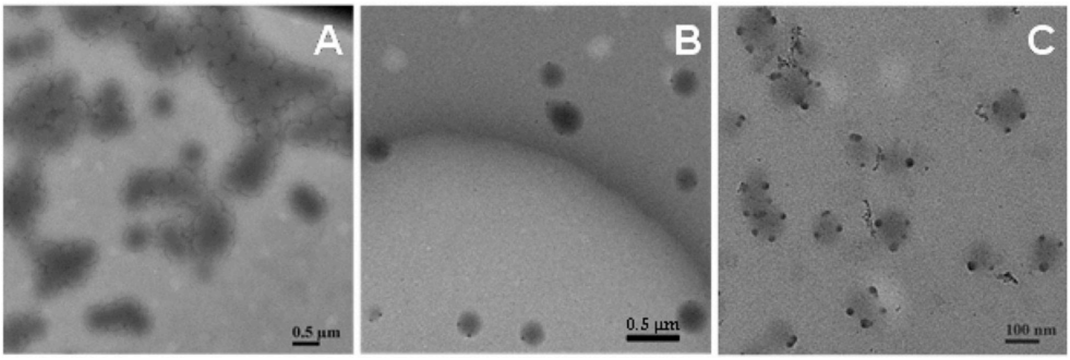

Figure 29. TEM micrographs of the RuO4 stained surfactant free poly(BA-co-MMA) particles produced by surfactant-free ab-initio free radical emulsion polymerization:

without Janus NPs (A); 1 wt% of Janus nanoparticles and 5 wt% Janus NPs (C). Reproduced from Ref. [8] with permission from the Royal Society of Chemistry.

4.2 Applications in biological sciences and drug delivery

There is an increasing interest in employing Janus nanostructures for biological sciences and drug delivery. The Lahann groups prepared Janus nanoparticles obtained by electrodynamic jetting of two liquid solutions containing immiscible polymers and reported the good biocompatibility with cells.[91-93] The Ying group prepared biocompatible magnetic-quantum dot heterodimers coated with silica which is potentially useful for specific imaging of live cells.[94] The use of cadmium-based quantum dots has however raises some environmental and health concerns. Thus Ying group developed hydrophobic Fe_3O_4-Ag heterodimer nanocomposites, which were subsequently functionalized with hydrophilic groups for live cells imaging with two-photon fluorescence microscopy.[95] Similarly, Sotiriou et al. prepared heterodimer Fe_2O_3−Ag nanoparticles encapsulated by a thin silica layer rendering the particles hydrophilic and biocompatible, facilitating their use as a potential biomarkers (Figure 30).[87]

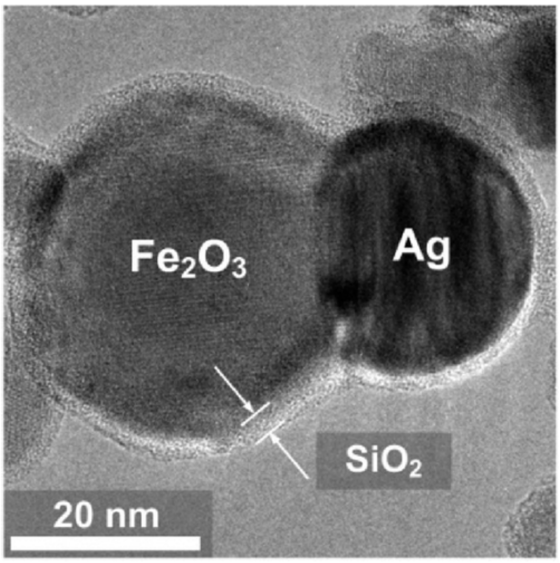

Figure 30. TEM micrograph of SiO_2-coated Ag/Fe_2O_3 sample. Reproduced with permission.[87] Copyright (2011) American Chemical Society.

Hu and Gao prepared polystyrene-magnetite Janus nanoparticles for dual applications of imaging and magnetolytic therapy.[96] The authors further demonstrated magnetic field modulated imaging and efficacy in cancer treatment. Wu *et al.* developed a new type of multifunctional cellular probe, Janus nanocoral composed of polystyrene and gold lobes. The gold lobe was used for imaging and the polystyrene lobe was functionalized with antibodies to target receptors for breast cancer cells, enabling the potential for both detecting and imaging. The polystyrene lobe might be used as a reservoir for therapeutic agents, making this nanocoral system a useful candidate for biomedical applications.[85] Along this line, Janus particles are attractive candidates for drug delivery owing to their unique structure of having two separate compartments which allows the transport of incompatible drug molecules on the same vehicle. Xie *et al*. prepared for the first time biocompatible Janus particles that were composed of the biodegradable polymer poly(lactic-co-glycolic acid) (PLGA) by using fluidic-based nano-precipitation. These particles were investigated for the dual delivery of a hydrophobic (paclitaxel), and a hydrophilic (doxorubicin hydrochloride) anticancer drug.[97] The results indicated the efficient release of both drugs from the Janus particles (Figure 31).

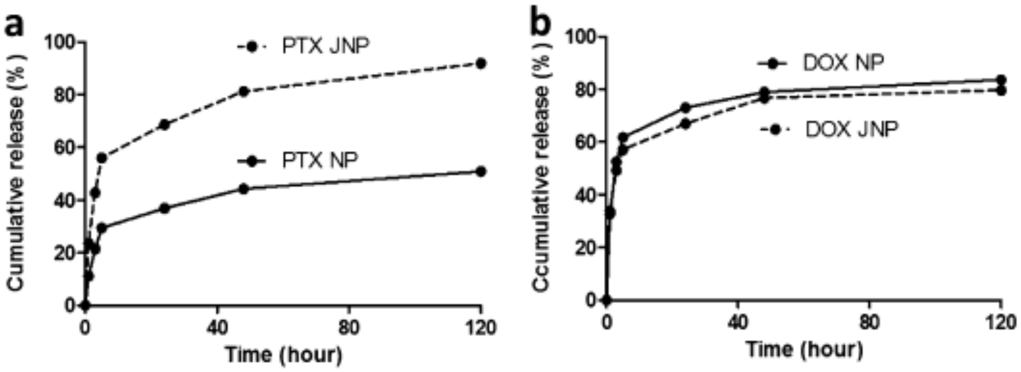

Figure 31. (A) Cumulative release of drugs from nanoparticles. (B) Release profiles of (A) PTX and (B) DOX from Janus nanoparticles (JNP) and homogeneous nanoparticles (NP) into phosphate buffer at 37°C. For each experiment, 2 g/ml of Janus particles and 1 mg/ml of homogeneous particles were used. DOX: Doxorubicin hydrochloride; PTX: Paclitaxel. Reproduced with permission.[97] Copyright (2012) American Chemical Society.

5. Conclusions and future perspectives

Janus particles have been shown to be smart materials presenting combined properties of different materials in one single unit. Janus particles have attracted great attention based on their asymmetric chemical composition and structure leading to their unique properties. Among the existing methods used for the synthesis of Janus particles, seeded emulsion polymerization is the most promising due to its low-cost, scalability and versatility. In addition, this method enables the synthesis of Janus particles at nanoscale length which is essential for certain applications such as drug delivery. Efforts are continuing to further increase the simplicity and versatility of the preparation of Janus particles in large quantities with tunable chemistry, suitable for the industrial applications. The self-assembly of Janus particles into hierarchal structures should be investigated more extensively as the properties of these complex structures could be as exciting as those of Janus particles. In addition, high-end applications of Janus nanoparticles such as painting, ceramics, and photonic materials need more attention from industry to transfer the laboratory scale to advanced technologies. For biomedical applications, the cell uptake mechanism of Janus nanoparticles is currently poorly understood, because existing studies have only focused on particles with uniform surface functionality. Therefore, there are still many exciting aspects of Janus nanoparticles to be explored for the development of a new generation of this unique material in the solution of real-world problems.

Acknowledgements

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