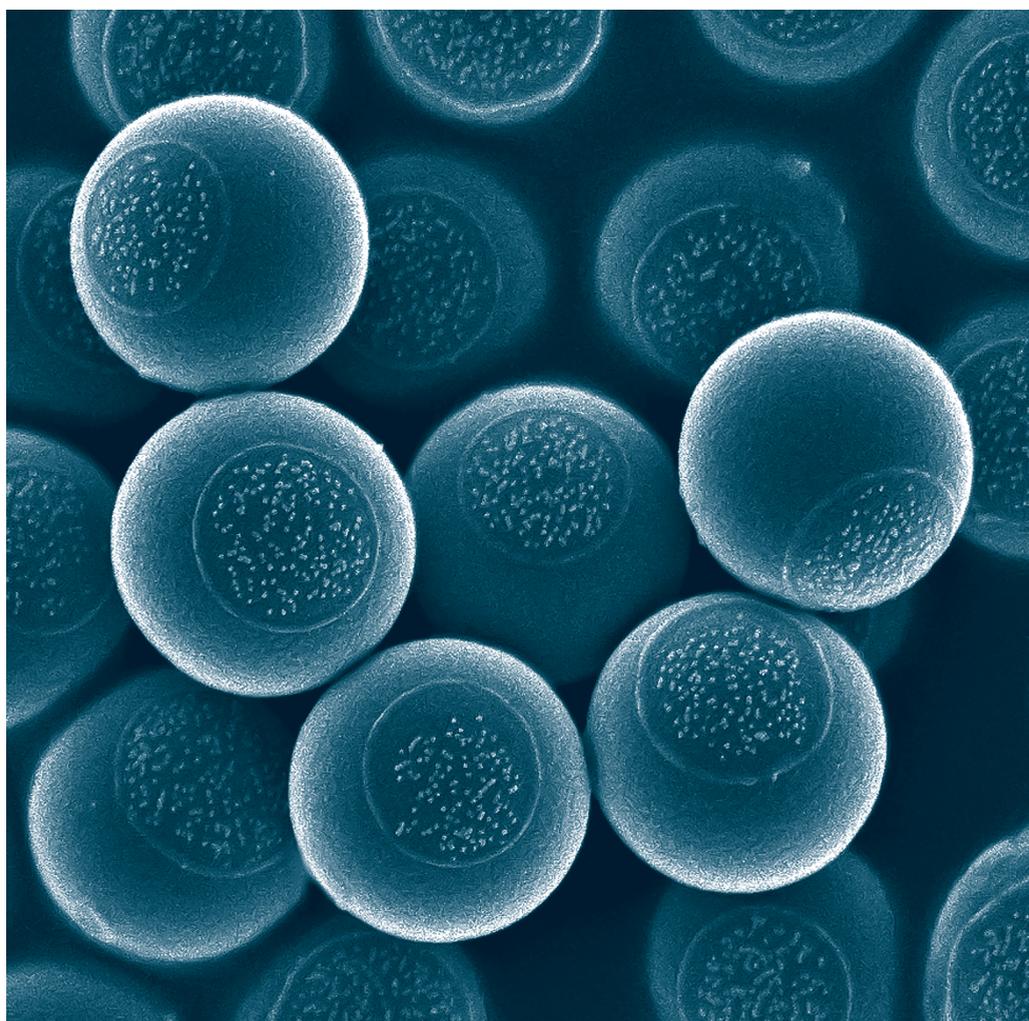


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Janus Particle Synthesis, Self-Assembly and Applications



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Janus Particle Synthesis, Self-assembly and Applications

Edited by

Shan Jiang

Massachusetts Institute of Technology, Cambridge, MA, USA

Email: sjiang2@mit.edu

Steve Granick

University of Illinois at Urbana-Champaign, IL, USA

Email: sgranick@illinois.edu

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Preface – An Introduction to Janus Particles

‘Janus’ is the name of an ancient Roman God, who has two faces peering into the past and the future, as shown in Figure 1a. Named after this Roman God, Janus particles have two distinguished surfaces/chemistries on the two sides, usually made of incompatible materials, such as hydrophobic *versus* hydrophilic and positive *versus* negative (charge). The idea of combining two incompatible properties into one object has precedent in an even earlier culture. In ancient Asian philosophy, it was believed that the seemingly opposite forces are interconnected in Nature and they give rise to the complicated change and transition in the world. The concept is called *Yin and Yang* (dark and bright) and symbolized in the classic Taoist Taijitu as shown in Figure 1b, which also looks like a Janus particle. So Janus particles can also be called ‘*Yin Yang*’ particles. Just as how *Yin and Yang* sheds light on the underlying principles of Nature, this book will demonstrate how Janus particles offer insight into fundamental science and lead to invention of new materials.

1 A Brief History

The first publication about Janus particles was written by Casagrande and Veyssey in 1988.¹ Pierre-Gilles de Gennes, Nobel Prize in Physics winner in 1991, reiterated the concept in the context of *soft matter* and made it known to the scientific community in his Nobel Laureate speech.² In de Gennes’s vision, Janus particles are the new materials that will adsorb on the water/air interface and form a monolayer with voids between them, which he called a ‘skin that



Figure 1 (a) Janus God image engraved on an ancient Roman coin; (b) Taoist Taijitu symbol used on the national flag of South Korea.

can breathe.’ It is interesting to note that in the same lecture, de Gennes identified fundamental commonality with polymers, liquid crystals and surfactants. He called attention to two characteristics shared by these vastly different systems: one is complexity, the other is flexibility. The Nobel Prize winner’s remark will again be proved true in this book. The complexity lies not only in the geometry and chemistry of Janus particles, but also in the assembly structures induced either by the interactions among particles themselves or by the external field. The flexibility is shown by the dynamics of the structures formed by these particles, *i.e.* how they diffuse in the bulk and adsorb at the interface. In the context of soft matter, side-by-side with block copolymers, liquid crystals and surfactants, Janus particles fit in perfectly as a colloidal version of these fascinating systems. de Gennes was entranced by the connection and had a vision of the new physics that Janus particles are bound to offer.

Soft matter studies blossomed in the following years. Rapid progress was made in polymers. Block copolymers became a hot topic and the phase diagram was mapped out both theoretically and experimentally. Various patterns generated from assembly structures were studied extensively and proposed for applications for different purposes. Liquid crystal studies also gained great momentum driven by the huge profit from industry. Surfactant research expanded through studies of phospholipids and lipid-like molecules. Making floppy liposomes, big or small, to mimic the cell membrane became popular in the laboratory and lipid-based formulations for drug delivery and biomedication also became widespread in both academia and industry.

However, Janus particle research lagged behind while other areas in soft matter were thriving. During the 15 years following de Gennes’s lecture, not much was done on Janus particles. The main obstacle in the field was the

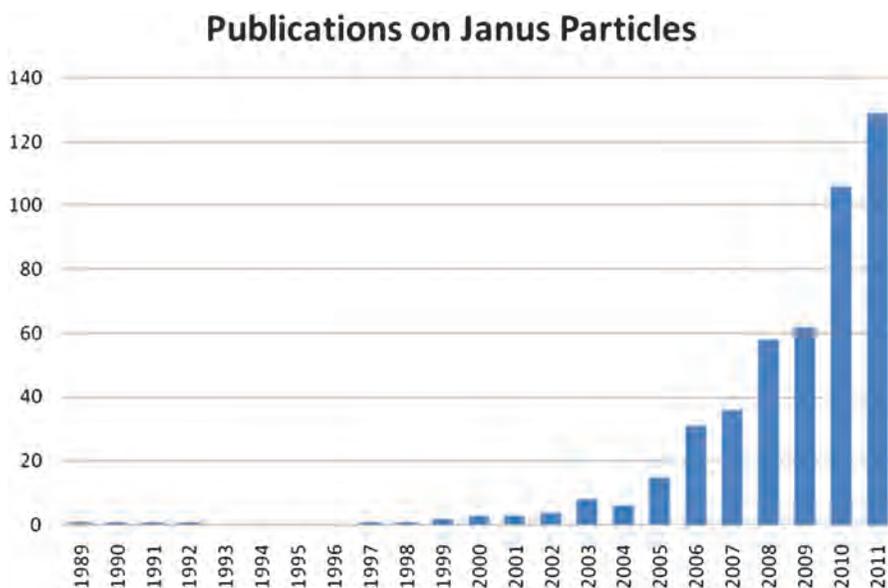


Figure 2 Statistics of publications on Janus particles from 1989 to 2011.

synthesis of these particles. People were searching for easy ways to fabricate Janus particles with well-defined geometry and chemistry. On the other hand, colloidal research has demonstrated many useful techniques to synthesize different particles in various sizes with homogeneous distributions. Enlightened by this progress, different methods for fabricating Janus particles started to emerge around 2003–2005. The momentum continued to build up in 2006 and the number of publications on Janus particles increased almost exponentially thereafter. The trend is still continuing today, as shown by Figure 2, based on article search in the database of Web of Science. The new methods of synthesizing Janus particles opened up the gate for further studies in the field.

2 How to Make Janus Particles

The first part of this book addresses the problem of synthesis. At de Gennes's time, the method was very limited in terms of control of size and geometry. One interesting suggestion is to modify the homogeneous particle surface to a different chemistry and then break the particles into fragments. In this way, all the fragments will adopt the Janus geometry automatically. This is an easy and low-cost approach. However, it only generates heterogeneous particles and offers no control over geometry. If the inner parts of the particles were fragmented, they would not be in Janus geometry and would be hard to separate out.

One of the early methods that successfully offered high-quality Janus particles is directional coating onto a monolayer of homogeneous particles deposited on a flat substrate.^{3,4} The size and dispersity of the particles are determined solely by the starting particles. Directional coating generates Janus particles with perfect 50% coverage. If the metal coating is deposited on fluorescent particles, ‘Moon particles’ can be obtained. Studies described in Chapter 10 (Stephen Anthony and Minsu Kim) tracked the rotation and diffusion of the Moon particles and studied the details of dynamics using Janus particles as a probe.

The directional coating method can be viewed as the particles themselves protecting one side that is not coated. Inspired by the protection approach, many other methods were developed. One very versatile approach is the emulsion-based method,⁵ taking advantage of the fact that particles were tightly adsorbed at the interface and partially protected by one phase. Janus geometry can be achieved by modifying the exposed side on the particles. This method can be simply scaled up since emulsions offer a huge amount of interface in a relatively small volume. What is more, the geometry of Janus particles can be fine tuned by adjusting how particles sit at the emulsion interface. The method is thoroughly reviewed in Chapter 4 (Chengliang Zhang, Wei Wei, Fuxin Liang and Zhenzhong Yang).

Protection and deprotection often require extra steps to achieve the Janus geometry. A more direct approach is simply to flow or stack two different materials together and form Janus particles. Chapter 3 (Tae-Hong Park and Joerg Lahann) describes the method of synthesizing Janus particles via electrohydrodynamic co-jetting. This method is similar to the microfluidic approach; however, the electric field induces particles of much smaller size. Chapter 5 (Joseph M. DeSimone, Jie-Yu Wang and Yapei Wang) describes a way to fabricate Janus particles using a special non-wetting mould. Both of these methods generate high-quality Janus particles with various geometries.

All the approaches mentioned above can generate micron or submicron particles; however, it is very challenging to fabricate small Janus particles below 100 nm. Synthesizing Janus particles of ultra-small size usually requires a special design or growing particles from scratch. Chapter 1 (Andreas Walther and Axel H. E. Müller) describes an ingenious way of synthesizing Janus particles using molecular assembly from block copolymers; Chapter 2 (Chao Wang and Chenjie Xu) discusses different ways of synthesizing fascinating dumbbell nanocrystals.

Table 1 summarizes some common methods used to synthesize Janus particles. However, this table is far from comprehensive and many more methods are being invented. Since details of these methods are discussed in the individual chapters, here we just give some guidelines for evaluation:

1. Homogeneity: whether particles are homogeneous in size and geometry.
2. Tunability: whether it is possible to change the shape and size of the particles and fine tune the Janus geometry.

Table 1 Common methods of synthesizing Janus particles.

<i>Method</i>	<i>Special device required</i>	<i>Size/distribution</i>	<i>Chemistry/materials</i>	<i>Production scale/scalability</i>
Molecular assembly	None	<100 nm monodisperse	Block copolymer assembly	mg easy to scale up
Nanocrystal dumbbell	High-temperature heating control device	<100 nm <10% dispersity	Metal or metal oxide coated with surfactants	mg easy to scale up
Microfluid	Microfluidic device	10–100 μm <5% dispersity	Photocurable monomers	mg hard to scale up
Electro co-jetting	Electrohydrodynamic co-jetting device	0.5–50 μm dispersity varies	Water-soluble polymers	mg difficult to scale up
Directional coating	Dielectric coating device	0.5–10 μm depends on starting particles	Metal and dielectric coatings	μg difficult to scale up
Emulsion	None	0.2–10 μm depends on starting particles	Particles with reactive surface	g easy to scale up
Lithography	Lithography device	0.5–100 μm monodisperse	Elastomer stamp and photocurable monomers	μg difficult to scale up

3. **Functionality:** whether it is easy to change materials of the particles and functionalize the surface.
4. **Scalability:** whether it is possible to scale up the procedure for large quantities.

Ultimately, ends dictate the means. For fundamental and assembly studies, we always want homogeneous particles with a tunable geometry; for emulsion stabilization, gram quantities of Janus particles are preferred; for drug delivery and biomedication, biocompatibility and biodegradability are the priorities.

3 What Can We Do With Janus Particles?

The second part of the book deals with this question – what can we do with Janus particles? Before answering the question, we can take a look at many fundamental biological structures that actually utilize the simple Janus motif. Nature has long been using the bottom up self-assembly approach to build up structures. For example, cell membranes are bilayers assembled from phospholipids, which are amphiphilic molecules with ‘Janus geometry’ of a charged hydrophilic head group and two hydrophobic tails. It has been observed in simulation that with the right geometry and interaction, Janus particles can self-assemble into bilayer structures.⁶ Another good example is DNA, which is given integrity by thousands of nucleotides, each of which consists of phosphate and nucleobase structures. Again, the simple Janus geometry of the nucleotide determines the DNA structure: hydrogen bonding between the nucleobases constructs the core to store the genetic information, while phosphates act as the backbone to protect the information. Analogous structures were also observed in the assembly of Janus particles.⁷ Chapter 9 (Yi Chen, Abigail K. R. Lytton-Jean and Hyuckjin Lee) shows beautiful examples of what self-assembly can achieve based on the specific binding of DNA molecules. Many elegant and unique structures were assembled, from crystals formed by Au nanoparticles with a DNA coating to crystal structures formed by DNA molecules themselves.

We can simply observe Janus particles. The first place in which people watched closely how Janus particles come together was not a bench-top experiment, but a computer simulation, in which perfect Janus particles can be created without too much trouble. Actually, simulation can create any geometry and shape of interest. The idea behind the simulation work is inspired by the concept of ‘colloidal molecules’,⁸ which first arose in the context of the packing of colloidal particles and the photonic crystal structures created by those particles. Clusters of simple colloids mimic those of small atoms and molecules with different shapes. Since the diffusion and assembly of colloidal particles are easily visible under an optical microscope, they can be used as a model system to study liquids, crystals, glasses and even atomic structures, which are hardly approachable in such detail at the equivalent single-atom or single-molecule level using conventional methods.

Janus particles can be viewed as one kind of fundamental colloidal molecule, whose molecular counterpart can be surfactant or dipolar molecules. Will Janus particles simply assemble in a way akin to how small molecules do? Can we create Janus particle micelles or even Janus particle liposomes? Theoretical work provides a good framework to solve these questions, as described in Chapter 6 (Achille Giacometti, Flavio Romano and Francesco Sciortino). To fully address the question also requires coordination between simulation and experiment. On the one hand, simulation can fully explore the possibility of Janus geometry and interactions that lead to different assembly structures. On the other hand, a simulation only makes good sense when the model can be realized in the experimental setup. There are also structures observed in experiments which can hardly be understood by just looking at them under the microscope. Only by combining experiment and simulation can we start to understand the underlying mechanisms. Chapter 7 (Liang Hong and Angelo Cacciuto) shows a perfect example of how experiment inspired simulation and simulation in turn helped understand experimental data. In that chapter, simulation actually further discovered new, previously unobserved interesting structures, based on the experimental feedback.

What we have learned is that some principles about assembly are indeed shared by both Janus particles and small molecules. Amphiphilic particles form clusters akin to micelles. However, there are also unique features which only exist in particle systems, such that the clusters adopt a specific geometry with a certain number of particles in the dilute regime. When the particle concentration increases, the clusters grow into long chains, with unique kinetics and stacking structures.⁹

Going beyond self-assembly, structures with different hierarchy can be forged when Janus particles are susceptible to the external field. Chapter 8 (Ilona Kretzschmar, Sumit Gangwal, Amar B. Pawar and Orlin D. Velev) discusses the details of how Janus particles respond and assemble under electric, magnetic and convective flow fields.

What else can we do with Janus particles besides assembly? Many hints can be taken from what is already known about small surfactant molecules and homogeneous colloids. Janus particles should stabilize emulsions as surfactant molecules can do. It is known that homogeneous particles can also stabilize emulsions with good stability. Theoretical calculation shows that the advantage of using Janus particles may show up when the particle size is ~ 10 nm, where the adsorption energy for homogeneous particles is close to the thermal fluctuation.¹⁰ Chapter 11 (Shan Jiang and Steve Granick) presents detailed discussions of this. Chapter 1 also shows one example where Janus particles were used for emulsion polymerization and led to a very homogeneous particle size distribution, which cannot be achieved by a conventional surfactant-stabilized emulsion system.

Janus particles can assist catalysis, as demonstrated in Chapter 2. Gold-oxide heterodimer crystals presented high catalytic activity over the traditional catalyst. The effect is due to electron transfer from the oxide to the Fermi level

of the supported Au nanoparticles.¹¹ Janus particles can also assist to deliver drugs. Different drugs can be loaded together on to one particle and be released simultaneously to achieve synergistic effects. Imaging modality can also be combined with a drug to serve as a theranostics (therapeutics and diagnostics) agent. However, careful investigation is definitely needed to show the true advantage of using Janus particles over simply mixing things together. Chapter 3 and Chapter 12 (Zhiyong Poon and Paula Hammond) present some nice examples of how Janus particles have been applied for biomedication purposes.

4 Perspectives

As shown in Figure 3, the majority of current research on Janus particles has been focused on synthesis (statistics based on publications through 2011). At the same time, it is nice to see researchers from different backgrounds contributing together to the field. With many methods of making Janus at hand, maybe it is time to think more beyond synthesis. A balanced development from theory, simulation and experiment would be the optimal approach.

Many of the details about Janus particles are not yet clear. What is their phase diagram? Will they form different crystal phases? How do they arrange themselves at an oil/water interface? How do Janus particles interact with cells and proteins?

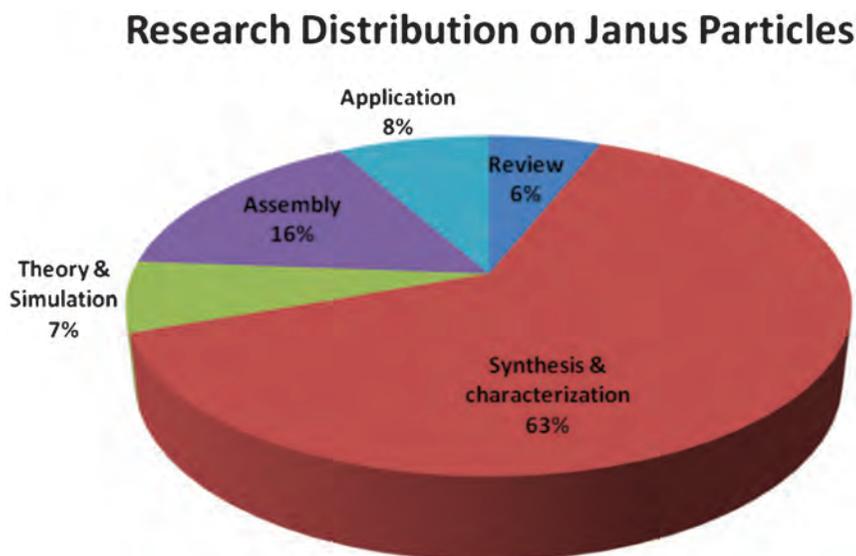


Figure 3 Statistics analysis of research topic distributed on Janus particles, based on the publications shown in Figure 2.

Again seeking analogy from what already happens in biology, is it possible to manufacture Janus particles like DNA molecules to store information or like proteins and enzymes to create lock-and-key structures, with more than just one patch on a single particle? How about Janus particles with different shapes? How about going beyond the simple Janus geometry and creating a triblock structure with patches on the two ends of the particle or at any location on the particle as we wish? Indeed, beautiful kagome lattice structures were created with the simple extension from two faces to three ('triblock').¹² The untapped possibilities with Janus and Janus-like particles are vast.

Wouldn't it be wonderful to have environmentally responsive Janus particles? Imagine if an assembled nanoparticle loaded with DNA, siRNA or drug molecules disassembles itself once the nanoparticle reaches inside a cell or a tumor site, in response to local change of pH or the presence of biomarkers. This may help kill cancer or cure diseases. Or imagine if a Janus particle can controllably stabilize and destabilize emulsions. This might help save the expense in harvesting oil from the deep sea.

Janus particles may not be the elixir to solve all these problems; however, the concept indeed offers an attractive new approach to solve many hard-to-tackle challenges. Janus particles may lead us to a whole new era of colloidal science research.

Acknowledgements

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Shan Jiang and Steve Granick
MIT and UIUC, April 2012

References

1. C. Casagrande and M. Veyssie, *C. R. Acad. Sci., Ser. II*, 1988, **306**, 1423.
2. P.-G. de Gennes, *Angew. Chem. Int. Ed. Engl.*, 1992, **31**, 842.
3. L. Petit, J. P. Manaud, C. Mingotaud, S. Ravaine and E. Duguët, *Mater. Lett.*, 2001, **51**, 478.
4. Z. N. Bao, L. Chen, M. Weldon, E. Chandross, O. Cherniavskaya, Y. Dai and J. B. H. Tok, *Chem. Mater.*, 2002, **14**, 24.
5. L. Hong, S. Jiang and S. Granick, *Langmuir*, 2006, **22**, 9495.
6. W. L. Miller and A. Cacciuto, *Phys. Rev. E*, 2009, **80**, 021404.
7. Y. C. Chen, V. Dimonie and M. S. Elsaesser, *J. Appl. Polym. Sci.*, 1991, **42**, 1049.

8. M. Giersig, T. Ung, L. M. Liz-Marzan and P. Mulvaney, *Adv. Mater.*, 1997, **9**, 570.
9. Q. Chen, J. K. Whitmer, S. Jiang, S. C. Bae, E. Luijten and S. Granick, *Science*, 2011, **331**, 199.
10. B. P. Binks and P. D. I. Fletcher, *Langmuir*, 2001, **17**, 4708.
11. L. M. Molina and B. Hammer, *Phys. Rev. Lett.*, 2003, **90**, 206102.
12. Q. Chen, S. C. Bae and S. Granick, *Nature*, 2011, **469**, 381.

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CHAPTER 1

Soft, Nanoscale Janus Particles by Macromolecular Engineering and Molecular Self-assembly

ANDREAS WALTHER*^a AND AXEL H. E. MÜLLER*^b

^a DWI at RWTH Aachen University, 52056 Aachen, Germany;

^b Macromolecular Chemistry II, University of Bayreuth, 95444 Bayreuth, Germany

*E-mail: walther@dw.rwth-aachen.de or axel.mueller@uni-bayreuth.de

1.1 Introduction

Macromolecular engineering has evolved into a powerful toolbox for the preparation of complex polymer topologies with remarkable control over both the architecture and the distribution of monomer sequences into, *e.g.*, block-type structures or well-defined branched macromolecules. The rapid advances in controlled/living polymerization techniques during the last two decades have greatly facilitated this development. In the context of Janus particles, macromolecular engineering is interesting not only for the direct synthesis of phase-segregated unimolecular objects, but also for harnessing the self-assembly capabilities of tailor-made polymers owing to mutually incompatible polymer blocks, solvophobic effects or specific molecular interactions. Indeed, self-assembly of block copolymers has proven to be a remarkably elegant strategy to generate polymer-based nano-objects, where we have seen progress to increasingly sophisticated soft nanoparticles, from simple diblock copolymer micelles and vesicles, to multicompartment micelles (MCMs) with increasingly

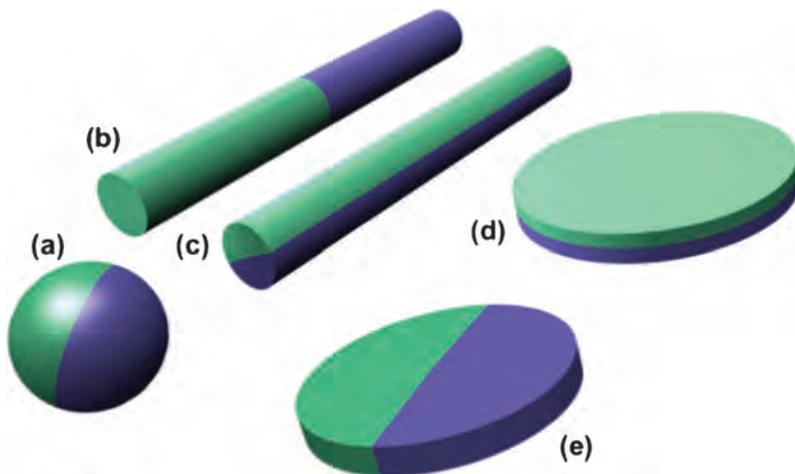


Figure 1.1 Different Janus particle topologies. Architectures (a)–(d) have so far been realized by synthetic and self-assembly approaches for nanoscale polymeric Janus particles.

complex geometries.^{1–4} Still, directly breaking the symmetry into biphasic Janus (Figure 1.1) particles or micelles has remained a considerable challenge.

Polymer-based Janus particles formed by direct synthesis or self-assembly of block copolymers are unique among this class of non-centrosymmetric colloids. First, truly nanoscale dimensions (i.e. <100 nm) can be approached that are very difficult to tackle by, *e.g.*, common desymmetrization reactions at interfaces or phase separation processes in emulsions, microfluidics or electrohydrodynamic jetting. Second, smart polymer segments, able to respond to environmental changes by phase transitions, impart a large-scale responsiveness to trigger superstructure formation or create strongly amphiphilic particles relevant for surface nanostructuring and the stabilization of interfaces. These properties render them a key building block for switchable materials. As a third criterion, polymers are also the crucial soft materials to communicate with the environment and to mediate interactions with cells, proteins and other living matter when approaching the biological interface with synthetic materials. Consequently, they are a valuable material class in the multitude of Janus particles available nowadays.

In this chapter, we review and discuss recent developments towards polymeric Janus particles. We place an emphasis on strategies specifically involving advanced polymer synthesis to create unimolecular objects and on methodologies utilizing self-assembly as well as post-transformations of self-assembled structures to create biphasic particles. Thereby, we focus on the small size regime and discuss particle architectures with different dimensionalities, in which at least one dimension is truly nanoscale (*i.e.* <100 nm). It may be noted that there are other approaches towards polymer-based Janus particles on the (sub)micron scale, such as phase separation in emulsion

droplets, lithographic approaches in microfluidic channels and electrohydrodynamic co-jetting, which are, however, beyond the focus of this contribution and are discussed in other chapters. This chapter is grouped into four topics. The first three are (a) Janus particles *via* direct macromolecular engineering, (b) Janus particles *via* direct self-assembly and/or transformations in solution and (c) Janus particles *via* transformation of self-assembled triblock terpolymer bulk structures. We finally discuss (d) self-assembly properties of the synthesized Janus particles and highlight some potential applications that have already been realized.

1.2 Janus Particles *via* Direct Macromolecular Engineering

The rapid advances in synthetic tools available to polymer chemists have triggered significant interest in the preparation of Janus particles. One of the earliest strategies involved the attachment or growth of different polymer chains to/from a single focal point or to/from a focal line with the aim of preparing spherical or cylindrical Janus particles, also known as heterografted star-shaped and cylindrical brush polymers. The resulting structures are outlined in Figure 1.2, which also highlights one of the major challenges for such nanoscale objects with high dynamics of the polymer chains. Phase separation of the chemically different polymer arms is required to realize a true Janus particle character in solution. However, phase separation for polymer arms emanating from a single focal point or from a dynamic micellar core – as will be discussed later – is not self-evident. It is governed by the interplay between entropy, favoring mixing of the polymer chains, and the enthalpic force of polymer chains to phase separate.^{5,6} In solution, the latter is drastically

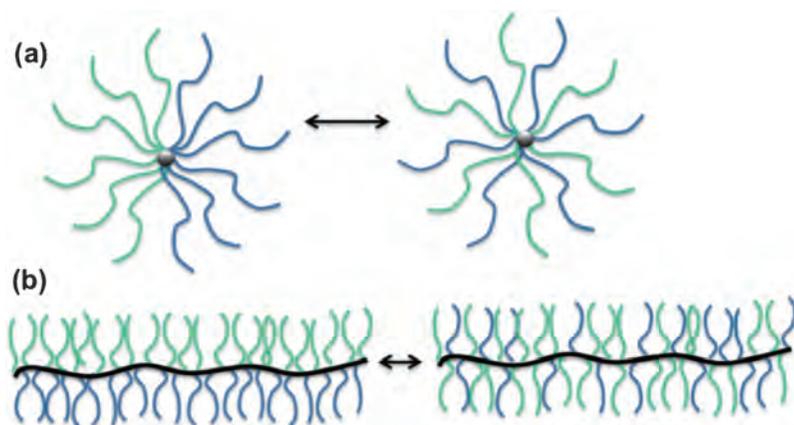


Figure 1.2 The interplay between entropy-favored chain mixing and polymer incompatibility-promoted phase separation: mixed and phase-segregated heteroarm grafted star-shaped (a) and cylindrical brush (b) polymers.

reduced compared with the bulk state and it has proven a challenging task to design systems that allow a freely occurring phase separation. In this context, it is also important to point to another major obstacle, namely the difficulty of providing solid *in situ* proof for corona segregation of polymer nano-objects in solution. The nanoscale dimensions and the often weak natural contrast of different organic parts for imaging are the main complications. This challenge can be best met by 2D ^1H - ^1H NOESY NMR (NOE = nuclear Overhauser effect), an NMR technique probing intermolecular distances *via* through-space coupling, or by direct (cryogenic) transmission electron microscope (TEM) imaging using suitable staining methods to augment the natural contrast.

Some of the first evidence that a phase separation in heteroarm star polymers can indeed occur was delivered by Kiriya *et al.*⁷ In their atomic force microscopy (AFM) investigations on a system of heteroarm star polymers composed of seven arms of polystyrene (PS) and seven arms of poly(2-vinylpyridine) (PS₇-P2VP₇), it was observed that different topologies of the molecules result upon deposition from different solvents on to mica (Figure 1.3). Chloroform (CHCl₃) led to a hat-shaped appearance, whereas tetrahydrofuran (THF) yielded a more globular shape. The dissimilar shapes were attributed to the adsorption of Janus-type conformations in the case of CHCl₃, whereas a mixed conformation was suggested for the molecules deposited from THF. These observations were supported by calculations of the solubility parameters, which confirmed that CHCl₃ is a more selective solvent for P2VP and thus can enforce intramolecular phase segregation and a Janus-type conformation in solution. One uncertainty related to the imaging of deposited molecules of dynamic species always lies in the unclear effect of the surface properties on the adsorption behavior, *i.e.* selective adsorption due to preferred adhesion – a problem hard to come by with *ex situ* techniques.

An improved focal point design was suggested by Ge *et al.*, who reported the synthesis and stimuli-responsive self-assembly of double-hydrophilic Janus-type A₇B₁₄ heteroarm star copolymers with two types of water-soluble polymer arms, poly(*N*-isopropylacrylamide) (PNIPAAm) and poly(2-(diethylamino)ethyl methacrylate) (PDEAMA), emanating from the two opposing sides of a rigid toroidal β -cyclodextrin (β -CD) core.⁸ Owing to the pre-encoded phase separation within the focal point, an enhanced tendency for phase separation of the two arms can be expected. The authors found an interesting schizophrenic self-assembly behavior. Depending on the conditions for triggering the solubility to insolubility phase transitions of the two polymer arms, which are high temperature for PNIPAAm and high pH for PDEAMA, it was possible to switch between two vesicle states by inverting the membrane structure. Such a vesicle inversion procedure is a highly unlikely scenario for simple coil-coil diblock copolymers and can serve as indirect evidence for the Janus character of these stars.

Zhu and co-workers described a facile and large-scale synthesis of possibly the smallest unimolecular Janus nanoparticles by intramolecular crosslinking of the inner P2VP block of a polystyrene-*block*-poly(2-vinylpyridine)-*block*-

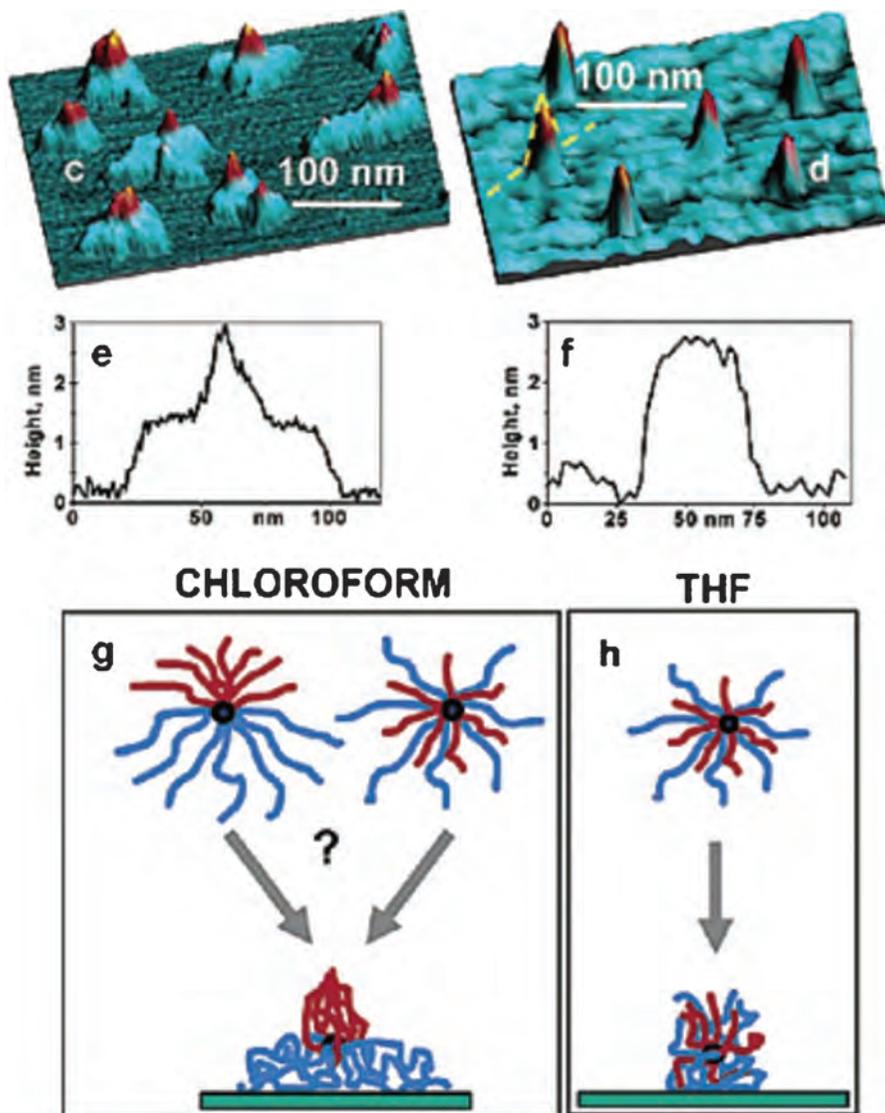


Figure 1.3 Solvent-induced transition from a mixed to a phase-separated structure in heteroarm grafted star polymers. Adapted with permission from *Macromolecules*, 2003, **36**, 8704.⁷ Copyright 2003 American Chemical Society.

poly(ethylene oxide) (PS-*b*-P2VP-*b*-PEO or SVEO) triblock terpolymer (Figure 1.4).⁹ Simple addition of an α,ω -dibromoalkane in a common solvent, dimethylformamide (DMF), resulted in nanoscale Janus particles with exactly one polymer arm of each end block attached to the central core. Interestingly, these Janus particles showed a concentration-dependent self-assembly beha-

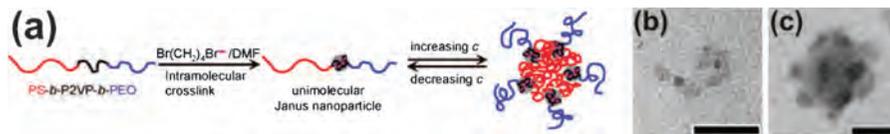


Figure 1.4 Ultrasmall Janus particles *via* intramolecular crosslinking of a polystyrene-*block*-poly(2-vinylpyridine)-*block*-poly(ethylene oxide) triblock terpolymer using a difunctional bromoalkane. TEM images of individual Janus nanoparticles and self-assembled aggregates resembling raspberry/football-shaped multicompartment micelles (scale bars = 50 nm). Reprinted and adapted with permission from *Macromolecules*, 2008, **41**, 8159.⁹ Copyright 2008 American Chemical Society.

rior into supermicelles upon reaching a critical aggregation concentration, c_{ac} , of $\sim 2 \text{ mg mL}^{-1}$. Strikingly, this aggregation also took place in a good solvent (DMF) for both end blocks, PS and PEO, which is a first example of the unusual and intuitively unexpected self-assembly behavior of polymeric Janus particles in good solvents for both corona hemispheres.

Moving from these 3D systems with overall spherical character to 2D systems with cylindrical architectures, one can identify various synthetic efforts targeting different types of copolymer bottle brushes. Various groups have reported cylindrical copolymer brushes of poly(2-(dimethylamino)ethyl methacrylate) (PDMAEMA) and poly(ϵ -caprolactone) (PCL), PS and polylactide (PLA) or PS and PEO with a statistical distribution of side-chains along the backbone (Figure 1.2b).^{10–12} Although these molecules showed clustering into some irregular aggregates upon exposure to selective solvents, there are no conclusive data and discussion on the potential Janus character of such structures. Simulations by de Jong and ten Brinke demonstrated that complete phase separation may only occur at very high incompatibilities of the two grafted polymers (similar to hetero-arm star-shaped polymers), as expressed by a large Flory–Huggins parameter, χ .¹³ It was further suggested that a well-defined Janus cylinder may only be reached at theta conditions for both blocks and for rigid backbones (Figure 1.5). For good solvents and highly flexible backbones, common to most synthetic comb-shaped polymers, the extent of phase separation is reduced and the molecules undergo bending into different shapes.

Schmidt and co-workers found differently bent shapes for cylindrical brushes composed of P2VP and poly(methyl methacrylate) (PMMA), when imaged with AFM after deposition from different solvents.¹⁴ After quaternization of parts of the P2VP segments and deposition from CHCl_3 and H_2O , strongly bent horseshoe and multiply bent, spiral/meander-type conformations were observed. The strong bending within the horseshoe structures was attributed to a basically quantitative phase separation along the main axis, whereas a patchy structure was ascribed to the meander-type patterns. Ishizu and co-workers reported imaging data on the side-by-side aggregation of cylindrical brushes obtained by polymerization of PS and PEO macromonomers during a very slow evaporation process of 1 week, starting from a THF–

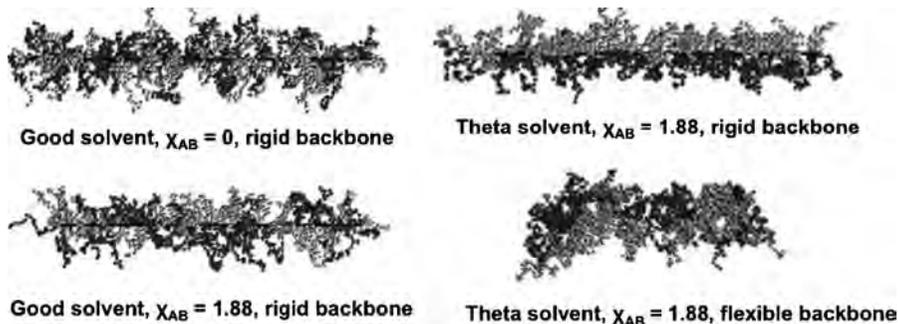


Figure 1.5 Snapshots of Monte Carlo simulations of hetero-grafted cylindrical copolymer brushes for high and low incompatibility of the side-chains, different solvent conditions and flexible *versus* rigid backbones. Reprinted and adapted with permission from *Macromol. Theory Simul.*, 2004, **13**, 318.¹³ Copyright 2004 Wiley-VCH.

water solution.¹⁵ These observations indicated that a reorientation can occur and that a biphasic character can develop if the correct solvent conditions (selectivity to drive self-assembly), concentration regime, and time scale are provided. These experimental systems and simulations, however, point to some limitations of this strategy when aiming at robustly phase-segregated two-dimensional cylindrical Janus brushes with corona segregation along the main axis. Further below, we will describe how to create similar Janus cylinders with very high precision using the controlled crosslinking of triblock terpolymer bulk phases.

Advances in polymer synthesis, however, have allowed the synthesis of a different type of cylindrical Janus particles. These are characterized by a phase separation perpendicular to the main axis into a cylindrical AB-type diblock brush.^{16–22} Such structures are typically obtained by consecutive block polymerization of macromonomers or by the polymerization of AB diblock copolymers with orthogonally reactive moieties in both blocks permitting side-by-side polymer-analogous attachment of preformed polymer chains (grafting to) or the growth of polymers *via* (parallel) grafting from reactions. A variety of AB-type Janus cylinders have been reported with widely different physical properties. For instance, Rzyaev *et al.* described in great depth the synthesis and structure formation of $\text{PLA}_{\text{comb}}\text{-}b\text{-PS}_{\text{comb}}$ AB-type Janus brushes with total molecular weights exceeding 1 MDa.^{21,22} Since the dimensions of the resulting lamellar bulk phases of the stiff AB cylinders approached the wavelength of visible light, a photonic bandgap behavior and an opalescent appearance could be observed for solid samples. Direct visualization by AFM was reported by Matyjaszewski and Sheiko and co-workers for their poly(*n*-butyl acrylate)_{comb}-*block*-PCL_{comb} (PnBA_{comb}-*b*-PCL_{comb}) AB diblock brushes (Figure 1.6) with amorphous and crystalline side-chains.²³

In addition, Deffieux *et al.* employed a multi-step reaction scheme to create $\text{PS}_{\text{comb}}\text{-}b\text{-polyisoprene}_{\text{comb}}$ ($\text{PS}_{\text{comb}}\text{-}b\text{-PI}_{\text{comb}}$) with glassy and liquid-like

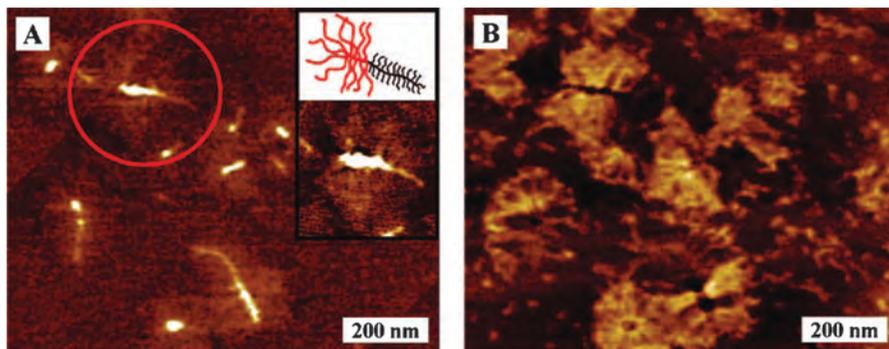


Figure 1.6 AFM images of heteroarm-grafted AB diblock Janus brushes with PnBA and PCL side-chains. (a) The height image displays single bottle brushes with a brighter PnBA head and a less distinct PCL tail. Verification of the PnBA and PCL assignment can be seen in the corresponding phase image (b). Reprinted with permission from *Macromolecules*, 2008, **41**, 6073.²³ Copyright 2008 American Chemical Society.

side-chains, thus further broadening the property range.¹⁶ Exposure to selective solvents such as heptane induced self-assembly into homogeneous and nearly spherical micelles. Similar self-assembly behavior was also reported for AB diblock brushes composed of PS and poly(acrylic acid) (PAA) side-chains.²⁴

In addition to the stepwise synthesis of unimolecular polymer objects *via* classical polymer chemistry, the desymmetrization of particles at interfaces has also reached the field of polymer-based nanoscale Janus particles. In general, toposelective modifications of immobilized particles are widely used to break the symmetry of inorganic particles and have greatly impacted the synthesis of Janus objects.

In the context of soft nano-objects, Chen and co-workers reported a simple one-pot process, in which they used PEO-*b*-P4VP-stabilized yttrium hydroxide nanotubes (YNTs, diameter ~ 200 nm and length 3–4 μm) as the interface for symmetry breaking. After initial formation of the polymer-coated YNT rods due to the adsorption of P4VP segments on the YNT surfaces *via* hydrogen bonding, a mixture of a radical initiator [azobisisobutyronitrile (AIBN)] in divinylbenzene (DVB) and additional NIPAAm was added to the dispersion (Figure 1.7).²⁵ Because of the solubility characteristics of the various compounds, AIBN and DVB accumulated in the P4VP phase, whereas NIPAAm remained dissolved in the continuous phase. Subsequent heating induced polymerization of the DVB in the confined space on the YNTs and nanoscopic, crosslinked polydivinylbenzene (PDVB) beads were formed due to the increased incompatibility of P4VP and PDVB polymers developing during the DVB polymerization. The radicals reaching the outer surface also initiated the NIPAAm polymerization, which led to the side-selective growth of PNIPAAm grafts, equaling an *in situ* desymmetrization. The collapsed state of the PNIPAAm during the thermal polymerization prevented the dissolution of the modified PDVB beads from the

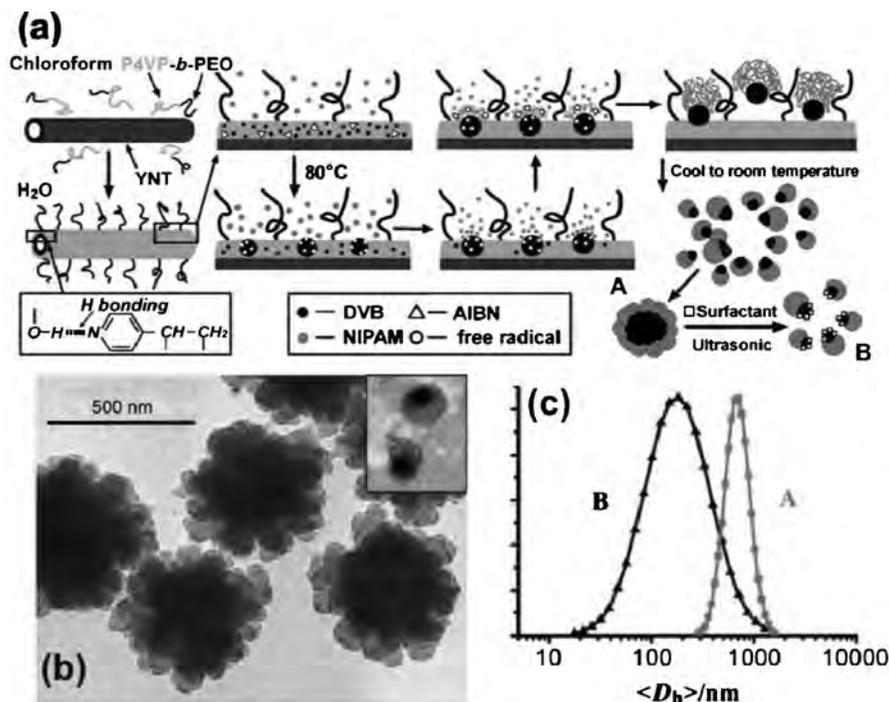


Figure 1.7 Reaction scheme illustrating the *in situ* desymmetrization of PDVB nanoparticles growing within the interfacial layer of water-dispersed polymer-coated YNTs. (b) TEM images of the supermicelles and of the individualized Janus particles (inset, same magnification). (c) DLS CONTIN plots of the supermicelles A and the individualized Janus particles after addition of surfactant. Reprinted with permission from *Angew. Chem. Int. Ed.* 2007, **46**, 6321.²⁵ Copyright 2007 Wiley-VCH.

YNTs. After resting at room temperature, the PNIPAAm/PDVB Janus particles separated from the polymer-coated inorganic rods. Dynamic light scattering (DLS) and TEM revealed flower-like aggregates of the strongly amphiphilic Janus particles with a hydrodynamic radius $\langle R_h \rangle_z = 320$ nm, which could be dissociated by the addition of excess surfactant to yield isolated Janus particles with an average radius of 80 nm. Interestingly, the process might be suitable for different monomers and could potentially be cycled using the same polymer-coated YNTs.

1.3 Janus Particles *via* Direct Self-assembly and Transformations in Solution

Solution-based self-assembly of block copolymers into micellar aggregates has rapidly developed throughout recent decades. It originally appeared fairly straightforward to design systems capable of leading to a Janus-type

conformation of micellar coronas. Systems conceived for that purpose involve ABC triblock terpolymers with an inner solvophobic block as micellar core and the A and C end blocks forming the corona. Additionally, a mixture of two diblock copolymers of the AB and BC type was expected to lead to feasible situations for Janus-type separation of the A/C corona and a common B core. Similar considerations for the phase separation of the polymer arms as discussed above for hetero-grafted polymers also apply. High incompatibility of the two A/C corona blocks and suitable solvent conditions are required (Figure 1.8a). Interestingly, however, Halperin calculated that a mixture of AB and BC will only lead to co-micellization into mixed micelles for low incompatibility of the two end blocks.²⁶ It was predicted that high incompatibility of both corona blocks would in fact lead to a set of two homogeneous populations of AB and CB micelles. Therefore, forced co-micellization of AB and CD diblock copolymers, carrying attractive interactions between the B and C blocks, was thought to be a viable alternative. The problem of uncertain co-micellization can be fully overcome for ABC triblock terpolymers possessing a chemical connectivity between the two corona blocks A and C.

A theoretical treatment of the corona segregation was presented by Charlaganov *et al.*, who used 2D self-consistent field theory (SCF) for an ABC triblock terpolymer system to calculate that corona phase segregation between A and C starts to occur at $\chi_{AC} \approx 0.5$ and leads to fully biphasic A/C coronas at $\chi_{AC} \approx 1$.⁶ Such a high degree of incompatibility between the two corona-forming blocks is yet difficult to achieve in the case of dissolved polymer segments in solution.

A number of groups, including ourselves, devoted significant effort to understanding and eventually mastering the challenge of fully phase-separating coronas within micellar systems. For instance, Hu and Liu²⁷ demonstrated that introducing adenine and thymine into the PCEMA segments of two diblock copolymers, poly(*tert*-butyl acrylate)-*block*-poly{(2-cinnamoyloxyethyl methacrylate)-*ran*-[2-(1-thyminylacetoxyethyl methacrylate)]}, PtBA-P(CEMA-T) and PS-*block*-PCEMA-*ran*-[2-(1-adeninylacetoxyethyl methacrylate)]}, PS-P(CEMA-A), leads to enhanced mixing of both chains in micelles due to H-bonding of the nucleic acid pairs. The observation of better mixing due to secondary interactions between both solvophobic blocks points to their significant incompatibility, as predicted by theory. However, despite the existing repulsion of both corona blocks, full segregation could not be obtained and different populations of patchy multicompartment micelles (MCMs) were found. Similar results were obtained by Zheng *et al.*²⁸ for a system of two diblock copolymers, PCEMA-*block*-poly(glycerol methacrylate) and PCEMA-*block*-PSGMA (PSGMA = succinated PGMA), with PCEMA forming the solvophobic core, and by Ma and co-workers^{29,30} and Kim *et al.*³¹ for a system using PNIPAm-*block*-P4VP and PEO-*block*-P4VP with a protonated P4VP as insoluble block or using stereo-complex formation of PNIPAAm-*block*-PLLA and PEO-*block*-PDLA, respectively.

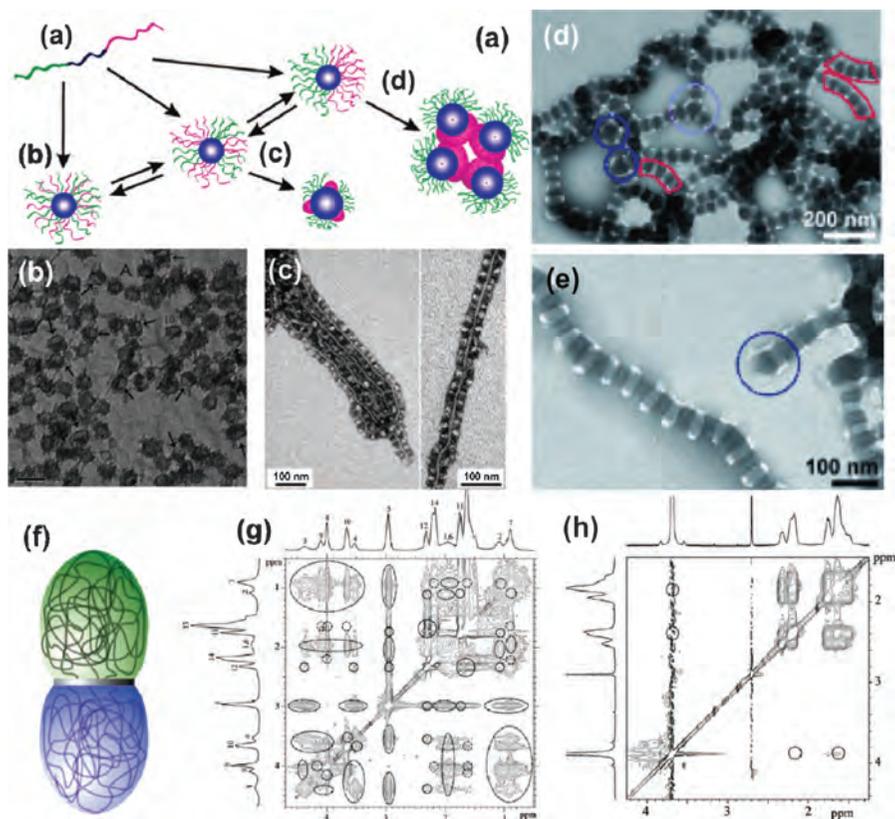


Figure 1.8 Direct self-assembly strategies for Janus micelles. (a) Possible corona configurations for triblock terpolymers with a solvophobic middle block and their superstructure formation upon triggering a solubility to insolubility transition on one of the end blocks. Reprinted with permission from *Langmuir*, 2010, **26**, 12237.³⁴ Copyright 2010 American Chemical Society. (b) Mixture of patchy multicompartment and Janus micelles obtained by direct dissolution of a poly(ethylene oxide)-*block*-poly(ϵ -caprolactone)-*block*-poly(2-aminoethyl methacrylate) (PEO-*b*-PCL-*b*-PAMA) triblock terpolymer in water, with PCL chains forming the micelle cores and the PEO and PAMA chains forming phase-segregated patchy or hemispherical coronas. The corona segregation was highlighted by selective silicification of the PAMA/PCL regions. Reprinted with permission from *Soft Matter*, 2010, **6**, 4851.³⁵ Copyright 2010 Royal Society of Chemistry. (c) Patchy worms formed by crystallization-driven self-assembly of a polystyrene-*block*-polyethylene-*block*-poly(methyl methacrylate) triblock terpolymer in organic media. PE forms the crystalline core and PS and PMMA phase segregate into a patchy corona. Reprinted with permission from *ACS Nano*, 2011, **5**, 9523.³⁷ Copyright 2011 American Chemical Society. (d, e) Superstructures formed in selective solvents (ethanol = non-solvent for *Pr*BS) by stacking of patchy multicompartment and Janus micelles composed of a fluorinated polybutadiene core and a compartmentalized corona of poly(*tert*-butoxystyrene) and poly(*tert*-butyl methacrylate). Different amounts of