5.1 Introduction

Because of their unique anisotropic characteristics, Janus particles have been assessed as attractive building blocks for self-assembly with desirable supramolecular architectures, leading to the creation of novel functional materials.¹⁻⁵ Janus particles with tunable chemistry and physical properties have attracted much attention in the fields of colloidal physics and chemistry for various applications ranging from optoelectronics, e-ink, drug delivery and bioimaging.⁶
Early synthetic strategies for generating Janus particles were focused on self-assembly and surface modification. So far, they are still popular as self-assembly can begin with a wide range of molecular moieties, including DNA and block copolymers, and surface modification is being extended to more and more mild reactions which hardly damage the particle interiors. Although the number of chemical compositions and surface chemistries utilized in these particle systems is increasing, particle shapes have been largely limited to a small number of simple geometries. Several recently developed top-down strategies have overcome this limitation and the creation of high-level structures has become possible. This chapter highlights the strategy of particle replication in non-wetting templates (PRINT) recently developed in our laboratories to fabricate monodisperse Janus particles with precise control over the size, shape, chemistry and distribution of the chemically distinct regions.

5.2 PRINT Technique

The history of the PRINT technique began with the synthesis of a new highly fluorinated perfluoropolyether (PFPE) elastomer by Rolland et al. in 2004. This photo-curable resin was demonstrated to have remarkably low surface energy (8–10 dyn cm\(^{-2}\)) with respect to other materials. In addition, possessing the properties of high gas permeability, high elastic recovery, good mechanical strength and high chemical and solvent resistance sets PFPE apart from the more commonly used polydimethylsiloxane (PDMS) as a template for micromolding. The PRINT technique is a soft lithography technique based on the use of PFPE molds that is able to mold most hydrophobic and hydrophilic liquids to generate useful materials in the form of arrays of patterned features, arrays of particles and isolated particles.

The PRINT process for fabricating isolated particles starts with an etched silicon master created using standard lithographic techniques in which the features are raised (Figure 5.1). The photo-curable liquid PFPE resin is then poured on to the silicon master and allowed to distribute evenly across and wet the surface of the master template. The resin is then photochemically cross-linked to form a robust elastomeric PFPE mold that is subsequently peeled away from the master to reveal micro- or nanoscale cavities on its surface. Next, a pre-particle solution is cast on a high surface energy sheet [typically poly(ethylene terephthalate) (PET)] using a Myer rod to form a uniform film of specified thickness. The sheet is then laminated to the empty PFPE mold using heat and pressure. When the high surface energy sheet is peeled away, capillary forces keep the liquid trapped in the mold cavities whereas excess solution is wicked away by the high surface energy sheet. The pre-particle solution in the filled mold cavities is then solidified using an appropriate means (UV light, thermal heating, lyophilization, etc.). Lastly, the solidified particles in the mold are removed by laminating the filled mold to a sacrificial harvesting film such as polyvinylpyrrolidinone, poly(vinyl alcohol) or...
cyanoacrylate. Peeling the harvesting film away from the mold results in an array of particles on the harvesting sheet. Free particles can then be collected by dissolving away the sacrificial adhesive film with an appropriate solvent for the adhesive and a non-solvent for the particles.

The PRINT technique has several attractive features that make it ideally suited for particle fabrication owing to the unique properties of the PFPE mold: (i) the low surface adhesion and elastic deformation of the PFPE mold facilitate the removal of the connecting flash layer, whereas other lithographic methods usually need an etching step to remove this scum layer; (ii) the highly fluorinated nature of the PFPE mold also facilitates the removal of particles from the mold; and (iii) PFPE has been shown to be compatible with a number of organic solvents that swell the traditionally used PDMS mold material, thus allowing PRINT to generate particles using a range of materials with very high fidelity to the original silicon master.

Another advantage of the PRINT technique is its scalability, allowing for the fabrication of monodisperse particles with precise and independent control over the particle size, shape and composition in relatively large quantities using roll-to-roll processing. In addition, the PRINT process is delicate and mild enough to be compatible with a variety of important cancer therapeutic agents, detection and imaging agents, various cargos (e.g. DNA, siRNA, protein, chemotherapy drugs, etc.), targeting ligands (e.g. antibodies, cell targeting peptides) and functional matrix materials (bioabsorbable polymers, stimuli-responsive materials, etc.). As a result, this new technique is really a platform technology that makes it possible to study the physical and chemical effects of particles in drug delivery, electronic devices, colloid science and other application areas.
Until recently, only particles composed of a homogeneous matrix had been fabricated. However, through some adaptations to the PRINT process, the fabrication of chemically distinct multicomponents segregated in a single particle has now been successfully achieved using the PRINT technology. As a result, the formation of two-component Janus particles and even particles with more than two chemically distinct regions with precisely controlled size and shape is now possible.

5.3 Janus Particles Fabricated by the PRINT Technique

Janus particles are fabricated through adaptation of the PRINT process using a multi-step mold filling operation. Through this adaptation, PRINT particles can be fabricated consisting of multiple compositions if two or more distinct materials are stepwise trapped in the same mold cavity at each filling step. Current studies of pre-particle materials for multi-step mold filling have been focused on photo-curable monomers. Depending on the dimensions of the mold features, the stepwise mold filling can occur in either vertical or horizontal directions. Ideally, one could anticipate partially filling the cavities in the PRINT mold with one component then in a subsequent step filling the rest of the cavity with a different chemistry to generate a Janus PRINT particle. In reality, though, it is difficult to partially fill the cavities uniformly. On the other hand, it is easy to fill the cavities completely with a composition that includes a diluent with a high vapor pressure that can be volatilized, leaving behind other components having a lower vapor pressure that could be partially cured followed by a subsequent step to “top-off” the mold cavities with a second component to create a Janus particle.

5.1.1 Stepwise Vertical Mold Filling

A typical process for vertically filling mold cavities to fabricate Janus particles is illustrated in Figure 5.2. In the first step, the mold cavities are filled with a photo-curable monomer solution in which the monomer has been dissolved in a volatile solvent. The solvent is then removed by evaporation and the resulting monomer is concentrated in the bottom of the mold cavities, thus leaving the mold partially filled. The monomer is then exposed to low-intensity UV irradiation and partially cured. In the partially cured state, the monomer still retains some photo-curable reactive groups but is solid enough to allow for a second filling of the mold cavity by another monomer without phase mixing. Both monomer phases are then completely photo-cured using intense UV irradiation, which results in the two different monomers being covalently bound together, inducing the formation of a Janus particle. The array of Janus particles can then be transferred from the mold cavities on to a sacrificial harvesting film as is done in the standard PRINT process. Free Janus particles with two distinct phases are finally obtained by dissolving away the sacrificial adhesive.
Figure 5.2  Fabrication of Janus particles using PRINT technology. (a) The initial monomer solution that has been diluted with a volatile solvent is filled into the mold; (b) after evaporation of the solvent, the remaining monomer is partially photo-cured; (c) another monomer is then filled into the partially filled mold cavities and both monomer phases are completely cured; (d) Janus particles are obtained after harvesting and purification. Reproduced from reference 20 with permission from the Institute of Physics.

Figure 5.3  SEM (top) and microscope (bottom) images of amphiphilic (left) and dipolar (right) Janus particles. Particles in the SEM images were harvested on a polycyanoacrylate harvesting layer. The microscope image of the amphiphilic Janus particles was obtained from the microscope fluorescent channel whereas that of the dipolar Janus particles was obtained from the overlaid image of the fluorescent and bright field channels. The scale bars in the SEM images represent 5 μm and in the microscope images 20 μm. Reproduced from reference 20 with permission from the Institute of Physics.
Early examples were constructed using a mold with a feature size of a $2 \times 2 \times 6$ \textmu m rectangular prism. Two-phase Janus particles were fabricated according to the previously described vertical two-step mold filling strategy.\textsuperscript{20} Amphiphilic Janus particles were obtained by combining a hydrophilic monomer [poly(ethylene glycol) monomethyl ether monomethacrylate, $M_n = 1000$ g mol$^{-1}$] with a hydrophobic monomer (lauryl acrylate). In addition, dipolar Janus particles were fabricated by combining a positively charged monomer (2-aminoethyl methacrylate hydrochloride dissolved in trimethylolpropane ethoxylate triacrylate) with a negatively charged monomer (acrylic acid mixed with trimethylolpropane ethoxylate triacrylate). The scanning electron microscopy (SEM) and optical microscopy images in Figure 5.3 clearly show the biphasic architecture of the resulting Janus particles. For better identification of the disparate regions in the Janus particles, one of the blocks was made fluorescent by doping with fluorescein o-acrylate while the other block without the fluorophore remained dark. By varying the concentration of the monomer in the monomer solution of the first block, the volume fraction ratio of the two different regions could be easily controlled.

5.1.2 Horizontal Stepwise Mold Filling

The stepwise mold filling fabrication of particles in the vertical direction is limited owing to two issues: (1) higher aspect ratio particles require a stronger force to pull the particles out of the mold cavities and (2) the etching of silicon master templates with a high aspect ratio pillar is very challenging. Because of these limitations, the multistep mold filling PRINT process has been extended to the horizontal direction as high aspect ratio particles that are lying down can be much more easily etched in silicon templates than vertically oriented high aspect ratio features.

Starting with a $20 \times 20 \times 240$ \textmu m rectangular rod as the starting template, a two-step mold filling process was developed to fabricate triphasic particles.\textsuperscript{21} First, a dilute solution of a photo-curable hydrophilic monomer in DMF was used to completely fill the PFPE mold. The solvent was then evaporated and the remaining monomer was drawn by capillary forces to the ends of the rectangular cavity. The monomer was then partially cured using a low-intensity UV light source to convert the monomer into a soft gel while leaving enough reactive groups to covalently bind subsequent blocks. Subsequently, the middle, empty cavity of the mold was completely filled with a second hydrophobic monomer. As shown in Figure 5.4, after the final monomer composition had been fully cured by intense UV irradiation, a triphasic architecture with the regions covalently connected together was obtained. The hydrophilic:hydrophobic ratio in the triphasic structure could be precisely tuned by simply changing the concentration of the original monomer solution. As shown in Figure 5.5, the hydrophilic heads of ABA amphiphilic triphasic rods could be controlled by varying the concentration of the first monomer.
mixture. Solely hydrophobic (Figure 5.5a) and hydrophilic (Figure 5.5b) particles were fabricated as reference samples.

The principle of fabricating triphasic rods has been extended to the generation of multi-region ABABA rods. In this technique, the mold is partially filled as before by first diluting a hydrophobic monomer solution containing a green dye. A second region is then generated using a dilute hydrophilic monomer solution containing a red dye (Figure 6a), while retaining an open space in the middle of the mold cavity which is able to be filled by a third hydrophobic monomer (undiluted) containing a green dye. As

Figure 5.4 Schematic illustration of the formation of triphasic rods and the corresponding microscope images of the molds in each step (all scale bars 100 μm). To distinguish the middle filled hydrophobic regions from the hydrophilic end regions, a photo-curable red dye and a green dye were premixed into the hydrophilic and hydrophobic monomers, respectively, prior to photo-curing. Reproduced from reference 21 with permission from the American Chemical Society.
shown in Figure 6b and c, five regions arranged as ABABA were observed to coexist in a particle, demonstrating this to be a powerful tool for building a library of anisotropic rods possessing tunable multiphases of different compositions.

Multiphase particles having either tri- or pentaphasic architectures are centrosymmetric. In order to fabricate asymmetric two-phase rods, centrifugal
force was used to pull the monomer from one end of the cavity to the other end after partially filling the mold with the first monomer. Typically, a partially filled mold containing two hydrophilic end regions was subjected to rotation around an axis perpendicular to the mold plane. As shown in Figure 5.7, the resulting centrifugal force drew the first monomer composition to the outer end of the mold cavity, leaving the rest of the cavity open. The open space was then subsequently filled with a second hydrophobic monomer, which after solidification via complete photo-curing yielded amphiphilic diphasic rods, as shown in Figure 5.8. In contrast to previous examples where the length of the initial region could be controlled by varying the concentration of the monomer solution, in this method it was observed that the length of the resulting initial region, on varying the initial monomer concentration from 30 to 80 wt%, was independent of the monomer concentration. Instead, the length of the initial region was found to be dependent on the rotational velocity as increasing the velocity decreased the region dimensions. Moreover, the length of the hydrophilic region remained unchanged as the rotation time was increased at a given angular velocity. This new technique could thus provide a strategy for constructing asymmetric particles of varying hydrophilic/hydrophobic ratios.

Figure 5.7  (a) Schematic illustration of the cross-section of the mold before and after rotation. Partially filled molds with a hydrophilic monomer containing a red dye dissolved in DMF solution at concentrations of 80 wt% before (b) and after rotation (c) at 14 000 rpm. Prior to rotation, the solvent was completely removed on a hot-plate at 70 °C for 30 min. Reproduced from reference 21 with permission from the American Chemical Society.
Stepwise mold filling in the horizontal direction can also be tailored to fabricate Janus particles with a diversity of particle shapes. Having mold cavities of non-centrosymmetric curvature concentrates the diluted monomer solution at the region having the strongest capillary effect. Several non-centrosymmetric features were attempted using the same synthetic route as previously described. As shown in Figure 5.9, Janus particles consisting of two separated phases with asymmetric dumbbell and tear-drop features were successfully fabricated. The first region containing a green dye is drawn into the region with a relatively smaller curvature, where stronger capillary force exists. This two-step filling process could certainly be applied to making Janus particles of other shapes.

As before, the ratio of the two regions in these asymmetric Janus particles could be tuned by adjusting the concentration of the initial monomer solution. The optical microscope images outlined in Figure 5.10 demonstrate a range of asymmetric Janus particles having tunable composition ratios.

Figure 5.8  Amphiphilic diphasic particles harvested on a harvesting film of cyanoacrylate, which were fabricated by filling the mold with 80 wt% of hydrophilic monomer solution and then rotating at various angular velocities, (a) 8000, (b) 10 000 and (c) 14 000 rpm, before being filling with a second hydrophobic monomer and cured. Images were captured by overlaying the images under red and green channels. Scale bar: 200 μm.

Figure 5.9  Fluorescent microscopy images of Janus particle arrays with asymmetric (a) dumbbell and (b) tear-drop shapes harvesting on a sacrificial film. Scale bar: 50 μm.
5.4 Patchy PRINT Particles

Many examples on selectively creating patches on particle surfaces by means of partially covering the particles have been reported. For example, patchy particle surfaces can be achieved either by trapping the particles at an oil/water interface or by arraying particles on a two-dimensional substrate. The PRINT technique is unique in its ability to fabricate more complex shapes rather than regular spheres. Using PRINT, patchy particles can be fabricated by surface modification of the solidified particle while either in the mold or on the harvesting layer. When particles are in the mold, one open face could be modified to form patchy particles. Once the particles have been transferred on to a harvesting layer, the other faces could also be modified. Surface modifications of the PRINT particles using chemical grafting and metal deposition have been attempted.

5.4.1 Surface-modified Particles by Chemical Grafting

Two particle shapes made using the PRINT process were selectively modified via chemical functionalization on one face. The particle shapes used were a 2 × 2 × 6 µm rectangular-prism and the other a 3 µm diameter hexnut. The particles were comprised of 67 wt% of the cross-linker PEG$_{428}$-triacrylate, 20 wt% of PEG$_{1000}$-monomethyl ether monomethacrylate, 10 wt% of the primary amine monomer aminoethyl methacrylate (AEM), 2 wt% of the fluorescent monomer fluorescein o-acrylate and 1 wt% of the photoinitiator 2,2-diethoxyacetophenone (DEAP). After photo-curing the monomer mixtures in the mold, the full mold with particles was inverted into a solution of buffered N-Hydroxysuccinimide (NHS)-rhodamine, which reacted with the primary amine group in the particles to introduce the rhodamine dye selectively on one exposed particle surface. The process is illustrated in Figure 5.11. After reaction, the molds were thoroughly rinsed with water and dried. The particles were then transferred out of the mold using cyanoacrylate and further washed with acetone for several times to remove the adhesive completely.

![Figure 5.10](image) Fluorescent microscope images of asymmetric particles demonstrating different domain ratios resulting from varied concentrations of the initial monomer solution. Scale bar: 20 µm.
The fluorescence microscopy images of the resulting particles with a selectively functionalized surface are shown in Figure 5.12. The particles clearly exhibit both green and red fluorescence. The green fluorescence is the result of the fluorescein o-acrylate incorporated into the bulk of the particles and the red fluorescence is from the surface-bound rhodamine dye.

5.4.2 Surface-functionalized Particles by Metal Deposition

In addition to chemical grafting to the particle surface while in the mold, selective vapor deposition of a metal can also be used to achieve chemical anisotropy on a particle surface. To prepare metal end-capped PRINT particles, a 10 nm layer of a Pd–Au alloy was sputtered on to the surface of a filled 2 × 2 × 6 μm rectangular prism mold. After coating, the particles were harvested by cyanoacrylate and purified. Scanning electron microscopy (SEM) and energy-dispersive X-ray spectroscopy (EDS) were used to confirm the presence of the metal alloy selectively on only one face of the particle surface (Figure 5.13). The metal-coated surface was brighter in the SEM image compared with the particle body. In addition, EDS analysis indicated the presence of the elements carbon and oxygen along the body of the particle whereas gold and palladium were identified only on the coated end.
5.5 Self-assembly of Janus PRINT Particles

Being able to fabricate particles comprised of two or more phases allows the opportunity to direct the self-assembly behaviors of these particles in solution or at an interface. The PRINT technique in particular allows for the fabrication of Janus particles with more complex geometries than the typically used simple spheres. A directed self-assembly study using 20 $\times$ 20 $\times$ 240 $\mu$m multiphase PRINT rods was conducted at a water/perfluorodecalin (PFD) interface to demonstrate the dependence of the self-assembly behavior on the particle architecture.\(^{21}\) The self-assembly of micron-sized particles at a water/oil interface is mainly attributed to the lateral capillary forces acting between the particles due to deformation of the oil/water interface.\(^{22\text{-}24}\) As controls, single-phase hydrophilic particles were shown to aggregate side-to-side into bundles (Figure 5.14a). The morphology of the assembled particles at the interface was studied using a gel trapping method which allowed replication of the oil/water interface on a cured PFPE film.\(^{25}\) The single-phase hydrophilic particles were found to reside on the oil/water interface with the particles projecting into the water phase. In this case, the particles could not be trapped in the oil phase as they were mostly confined by the water gel phase. As shown in Figure 5.14c, the interfacial distortion indicative of a negative meniscus on the oil surface was replicated. As a result, the hydrophilic particles tended to

![Figure 5.12](image-url)
interact over more of their perimeter in a side-to-side fashion, leading to a more pronounced reduction of the total energy at the interface. In contrast, the single-phase hydrophobic particles adopted a tip-to-tip aggregation at the water/PFD interface, forming a branched network (Figure 5.14b). Unlike the hydrophilic particles, the hydrophobic particles preferred wetting by the oil. As shown in Figure 5.14d, the hydrophobic particles contacted the oil phase by a rectangular long edge corner with nearly half of the perimeter projecting into the oil phase. Owing to this particular surface wetting phenomenon, the long sides of the particles have less excess area than the ends, hence the capillary attraction resulting from the elimination of excess area is stronger at the particle tips. As a result of the relatively weak attraction between the long sides, conventional steering breaks the metastable side-to-side aggregates, allowing the formation of branched structures with minimum energy in a tip-to-tip manner.

The self-assembly of amphiphilic tri- and diphasic rod particles was also investigated at the water/PFD interface. The triphasic particles, behaving like
bolaamphiphiles, preferred a side-to-side assembly, forming ordered ribbon structures at the interface, as shown in Figure 5.15a. With regard to the particle orientation at the interface, a very similar lateral capillary force to single-phase hydrophilic particles is assumed to provide a driving force in this directed self-assembly process. However, the triphasic architecture allows each particle to match the others in a better side-to-side fashion than does the single-phase hydrophilic particle. It is the difference in interfacial distortion around the hydrophilic and hydrophobic regions that limits each region of the triphasic particles to direct the assembly only with others having similar composition. It was observed that the triphasic particles adopted a bent conformation at the interface. This is presumably caused by the curved interface between the hydrophilic and hydrophobic regions and the swelling of

Figure 5.14  Fluorescence microscopic images of different particles assembled at the water/PFD interface for the (a) hydrophilic and (b) hydrophobic particles. Scanning electron micrographs are shown for the (c) PFPE mold obtained for the particle trapping experiment for the single-phase hydrophilic particles on the oil surface and (d) PFPE mold for the single-phase hydrophobic particles trapped at the oil phase. Self-assembly models are illustrated for the (e) hydrophilic and (f) hydrophobic particles at the water/oil interface. Reproduced from reference 21 with permission from the American Chemical Society.
the hydrophilic regions in water. Interestingly, the diphasic particles, having an asymmetric structure similar to a molecular surfactant, self-assembled into a 2D bilayer structure at the water/PFD interface (Figure 5.15b). In a bilayer structure, the side-to-side lateral interactions pull the particles together forming bundles while the heads of the hydrophobic regions tended to aggregate by a tip-to-tip lateral interaction. The cooperation of both assembly fashions thus induces the formation of a bilayer structure, being like the shell structure of vesicles assembled by traditional surfactants.

5.6 Conclusion and Future Perspectives

The PRINT technique is a leading technology for the fabrication of particles with precise control over the geometry and composition. The synthesized particles represent a new paradigm for assembling nanoscale materials into microscale structures, creating opportunities in optoelectronics, reinforcement and encapsulation/release strategies. Two-phase Janus particles and also multiphase particles have been shown to be able to be easily fabricated via a
multi-step mold filling adaptation of the PRINT technique, thus allowing precise control over the particle phases. Traditionally, numerous questions in the field of colloid physics and chemistry are encountered because of the limitations in particle geometry. Multiphase PRINT particles are now able to provide a platform to study the effects of composition and particle geometry on particle–particle interactions in colloid science. The ability to fabricate multiple components within a single particle is anticipated to open up avenues to new drug carriers, allowing the encapsulation of several drugs within hydrophilic or hydrophobic phases in one carrier. In addition, it is envisioned that the internalization of particles into the various types of cells could be realized using particles with a Janus architecture.

Janus particles with complex non-spherical architectures provide the possibility of obtaining novel self-assembled hierarchical superstructures which show great potential in medical and optoelectronic devices. Being able to fabricate nanoscale non-spherical Janus particles, although more challenging than the fabrication of micron-sized particles, is very attractive for a host of research fields.

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