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R E V I E W

Microfluidic Methods in Janus Particle Synthesis

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Abstract: Janus particles have been at the center of attention over the years due to their asymmetric nature that makes them superior in many ways to conventional monophase particles. Several techniques have been reported for the synthesis of Janus particles; however, microfluidic-based techniques are by far the most popular due to their versatility, rapid prototyping, low reagent consumption and superior control over reaction conditions. In this review, we will go through microfluidic-based Janus particle synthesis techniques and highlight how recent advances have led to complex functionalities being imparted to the Janus particles.

Keywords: anisotropy, droplet-based, asymmetric, nanoparticles, multi-functionality

Introduction

Over the last two decades, scientists have been drawn to the field of nanotechnology in search of novel smart materials with tailored qualities and desired capabilities. The principal aim was to lower the length scale at which matter was handled in order to obtain unprecedented control over material properties. In this context, Janus particles were studied extensively due to their anisotropic nature. The fact that such particles had different physical, chemical and surface properties along different orientations gave rise to exciting prospects in several applications,[1–6] including but not limited to cell encapsulation and assembly,[7] DNA assays,[8] biological multiplexing,[9] targeted drug delivery,[10–15] noninvasive imaging,[16] theranostics,[17,18] microlenses,[19–21] reflection-mode displays,[22] removal of organic and metal pollutants,[23,24] and water decontamination.[25,26] Since anisotropic particles possess remarkable potential, it was understandable that a large number of methods were reported for their synthesis.[27] Janus particle synthesis methods can be broadly classified under three categories, namely masking, phase separation and self-assembly.[28–31] Masking method involves immobilizing particles onto a template to block one side, followed by modifying the free side which leads to anisotropy; however, it is a laborious, multi-step process. The phase separation method consists primarily of three steps: dispersion of immiscible polymers in an emulsion, evaporation of the solvent and cross-linking to lock the polymer phases in place. In the self-assembly method, block copolymers are dispersed in a solvent, and assembled through solvent exchange followed by cross-linking of the core. Although phase separation and self-assembly methods are promising techniques, particles' size distribution is a problem if the particles are synthesized using a batch synthesis route.[1,32]

Apart from these conventional batch synthesis techniques, several research groups reported synthesis of Janus particles utilizing microfluidic systems to obtain multiple functionalities. In its broadest definition, microfluidics is the study of fluid flow inside channels having less than 1 mm characteristic length. Its main advantage is the capability to use small amounts of sample in detection, analysis, separation and synthesis with higher throughput and sensitivity. At this scale, it is easier to manipulate reagents in a more controllable way with reduced thermal and concentration gradients. It enables each reagent solution to go through an identical process, eventually reducing the variation of size and morphology. In terms of particle synthesis, microfluidic-based devices, due to this high level of control, provide the ability to fabricate monodisperse particles that have a narrow size distribution as compared to particles obtained with batch synthesis techniques.

Flow in a microfluidic system can be continuous or droplet-based. In continuous flow reactors, reagents flow directly inside the channel. On the other hand, in droplet-based microfluidics, reagents move within a channel in the form of nanoliter sized droplets, carried by another immiscible fluid. The droplets move inside the device without getting attached to the device walls due to the presence of a continuous phase between the droplets and the microchannel walls, which reduces channel contamination.

Microfluidic systems have been used for nano- and microparticle synthesis extensively due to their ability to precisely control reaction conditions, such as temperature, concentration, and residence time, which in turn alters nucleation and growth of the particles.[33,34] To synthesize Janus particles, two types of materials need to be brought together within the channel. This can be achieved by utilizing a channel design that merges two reagents together either inside a droplet or directly mixing in continuous flow. Several successful microfluidic approaches have been developed. The most popular ones are co-flowing streams, phase separation, double-emulsion, and electrohydrodynamic co-jetting methods.[32,35–37] In this review, these techniques will be described as separate subsections, and recent advances in Janus particles synthesis using these methods will be highlighted. Moreover, several other techniques were reported recently; for example, coagulation of nanoparticles inside droplets, controlled merging and crosslinking of droplets and using droplets as particle templates. These techniques do not directly fall under any of the main categories and they will be covered as a separate subsection entitled "miscellaneous techniques".

Co-Flowing Streams

In a microchannel, fluids with different chemical compositions can flow parallel to each other without mixing. This is due to the viscous forces that suppress diffusion. Fluid flowing in this configuration is named co-flowing streams. For the synthesis of Janus particles, two or more co-flowing streams are separated into droplets by the shear force exerted by another fluid stream and these droplets are later polymerized by UV exposure,[38,39] thermal curing or ionic crosslinking.[40,41] The co-flowing streams can be miscible or immiscible. Firstly, we will discuss miscible streams. Nisisako et al were the first to demonstrate the synthesis of hemispherical colored droplets and microspheres using this technique.[42]

Shepherd et al contributed to the fundamentals of co-flowing streams technique by synthesizing spherical- and discoidal-shaped Janus hydrogel granules by altering the cross-sectional geometry of the microchannels as shown in Figure 1.[43] The maintenance of a clear boundary between the co-flowing streams, and consequently in the generated droplets, depends on the ability to avoid convective and diffusive mixing. These findings were utilized by several other studies on Janus particle synthesis to obtain different kinds of anisotropies such as amphiphilicity,[11] optical anisotropy,[44,45] and magnetic anisotropy.[46,47] Hessberger et al reported synthesis of a liquid crystalline elastomer containing Janus particles using side-by-side capillaries.[45] The presence of liquid crystalline elastomer at one half of the Janus particles was shown to enhance the actuating properties of the particles in several applications. Maeda et al used a centrifuge-based microdroplet generator to fabricate Janus particles having magnetic anisotropy.[48] Seiffert et al reported the synthesis of Janus microshells (hollow) and microgels using three co-flowing streams. For these microshells, they used a non-polymerizable phase as the middle stream, which was removed later by washing, and for the microgels they used a polymerizable phase having magnetic nanoparticles, which provided the microgels with a magnetic core.[49] Xie et al utilized a nanoprecipitation method to synthesize sub-micrometer sized Janus particles capable of carrying payloads with different solubility in their two hemispheres.[11] Kamperman et al reported the production of multienzymatic microreactors having magnetic anisotropy using in-air micro-fluidics, where the co-flowing streams were transported in air instead of a conventional continuous phase fluid and were simultaneously cured by a cross-linking jet showered at the generated droplets.[50] They claimed that in-air microfluidics approach increased the production rate by two to three orders of magnitude compared to the conventional microfluidic approach. This work could potentially lead the way to high throughput synthesis of Janus particles, which has been the major challenge in commercialization of droplet-based microfluidic methods to synthesize particles. Their device and the obtained microparticles are shown in Figure 2. In a more recent work, Liu et al demonstrated the synthesis of hydrogel microparticles having magnetic anisotropy via an emulsion-based external gelation method. The set-up consisted of a pair of parallel flowing dispersed phase streams, one containing sodium alginate solution and the other containing a mixture of sodium alginate solution and magnetic nanoparticles, sheared into droplets that were solidified downstream by ionic cross-linking after reacting with calcium ions present in the cross linking agent flowing downstream.[51] This recent approach overcomes the shortcomings of the earlier ionic crosslinking method proposed by Zhao et al using a continuous stream of cross-linking agent
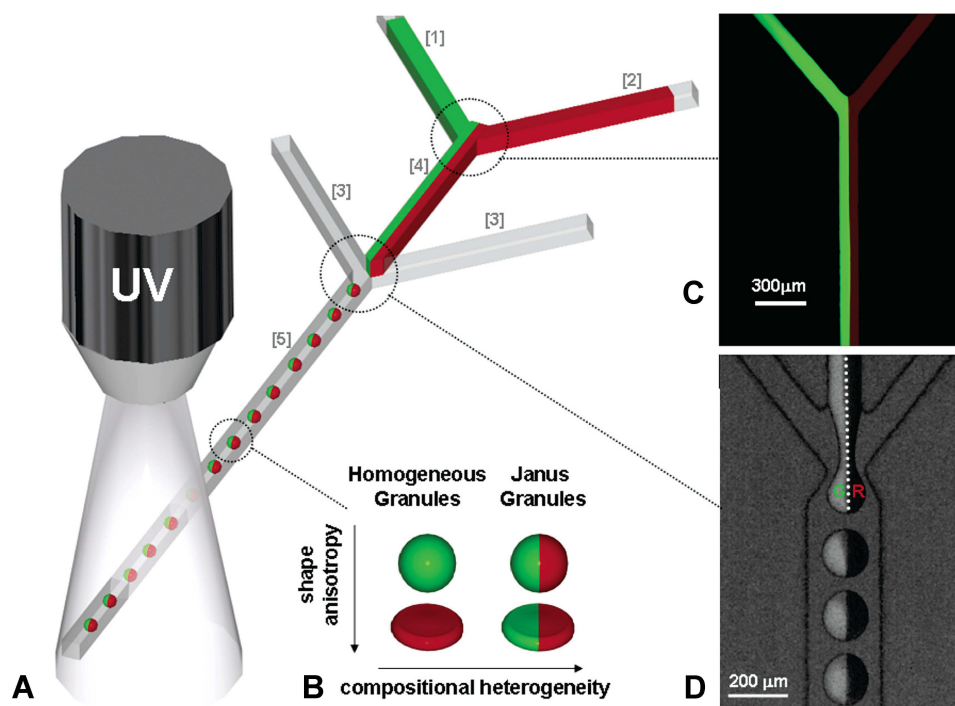
Figure 1 An example of a co-flowing microfluidic method to generate Janus droplets. (**A**) Schematic of the droplet generation process and subsequent polymerization. A mixture of an acrylamide, a cross-linker and a photoinitiator is injected from inlet 1 and 2. The fluids injected from inlet 1 and 2 contain different fluorescent materials. Mineral oil is injected from inlet 3. (**B**) Chart showing the variety of particles synthesized using this technique. (**C**) Fluorescent image of the parallel flowing streams showing the maintenance of a clear interface between the two streams. (**D**) Micrograph of the droplet generation process.
Note: Reprinted with permission from Shepherd RF, Conrad JC, Rhodes SK, et al. Microfluidic assembly of homogeneous and janus colloid-filled hydrogel granules. *Langmuir*. 2006;22(21):8618–8622. Copyright (2006) American Chemical Society.[43]
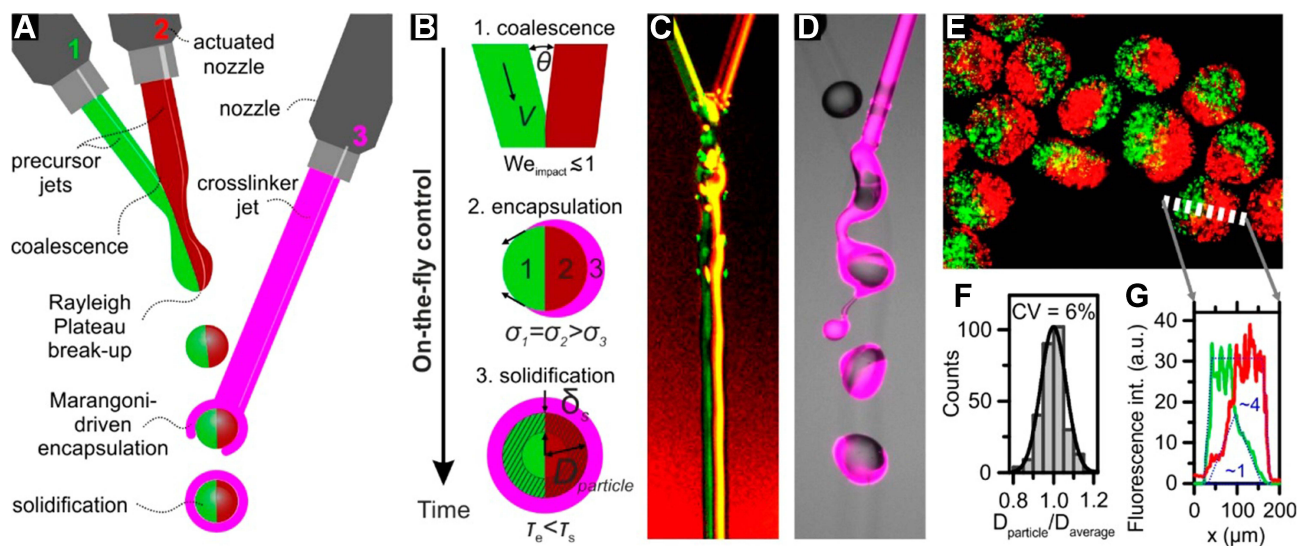

Figure 2 Janus particle generation in air microfluidics. Hydrogel particles with a paramagnetic compartment were synthesized at high throughput compared to channel based microfluidic systems. The size of these particles could be tuned, and the technique allowed monodiperse particle synthesis. Enzymes were encapsulated inside these particles and they were proposed as enzymatic bioreactors. (**A**) Concept of the device, (**B**) formation steps of the of the Janus particles, (**C** and **D**) real-time images during particle synthesis, (**E**) synthesized Janus particles under the fluorescent microscope, characterization results of the particles show that (**F**) the particles are monodisperse and that (**G**) there is a clear distinction between the two compartments.
Note: Reprinted from Kamperman T, Trikalitis VD, Karperien M, et al. Ultrahigh-throughput production of monodisperse and multifunctional janus microparticles using in-air microfluidics. *ACS Appl Mater Interfaces*. 2018;10(28):23433–23438. Creative Common.[50]

instead of droplets, and therefore, produces monodisperse uniform shaped spherical particles having a clear interface between the two hemispherical compartments.[47]

Co-flowing fluids used for the synthesis of Janus particles can also be immiscible. In this case, the structure of the Janus droplet, and in turn, of the particle, is determined by the spreading coefficient. The spreading coefficient is given by $S = \gamma_{AB} - (\gamma_A + \gamma_B)$,[52] where γ_{AB} is the interfacial tension between the two co-flowing phases, γ_A is the interfacial tension between the co-flowing phase A and continuous phase fluid, and γ_B is the interfacial tension between the co-flowing phase B and continuous phase fluid.[53]

The first report on the synthesis of Janus particles using immiscible co-flowing streams was presented by Nie et al where they synthesized Janus and ternary (trisectioned) particles. They also demonstrated the synthesis of Janus particles with varying ratios of two monomer streams.[54] Their device and obtained results are shown in Figure 3. Nisisako et al reported the synthesis of truncated Janus particles using one polymerizable and one non-polymerizable fluid as the co-flowing fluids.[40] After off-chip UV curing, the non-polymerizable phase was washed and a truncated Janus particle, whose shape was controlled with the interfacial tension, was produced. This technique of having a polymerizable and a non-polymerizable phase has been used in several works. Yu et al utilized this technique to synthesize truncated-, crescent- and hollow-shaped anisotropic colloidal photonic crystal supraparticles for potential use in novel color displays.[38] Some other uses of this approach are the two works of Nisasako et al where they fabricated a biconvex microlens using two co-flowing streams and biconcave microlens using three co-flowing streams.[20,21] Another interesting example of this technique is the synthesis of self-propelled micromotors for water decontamination, which was achieved by controlled decoration of Ag nanoparticles on the concave surface, TiO_2 nanoparticles on the convex surface and magnetic nanoparticles inside the micromotor itself.[25] Another interesting study to lay the foundation for other works was reported by Prasad et al where immiscible monomers in a co-flowing system were used to fabricate Janus particles with a dumbbell or a snowman shape depending on the capillary number of each stream. The dumbbell-shaped particles were incorporated with magnetic nanoparticles in one half, followed by a heat treatment to produce concave ceramic hemispheres having different surface textures and magnetic anisotropy.[55]

Yang et al utilized a side-by-side capillary configuration to synthesize anisotropic magnetic Janus particles where the anisotropy was maintained by having immiscible co-flowing streams.[56] Xu et al reported the synthesis of hydrophilic-hydrophobic anisotropic Janus particles using a selective channel surface modification. The surface of the dispersed phase microchannel was modified to make one side of the microchannel hydrophobic and the other side hydrophilic.
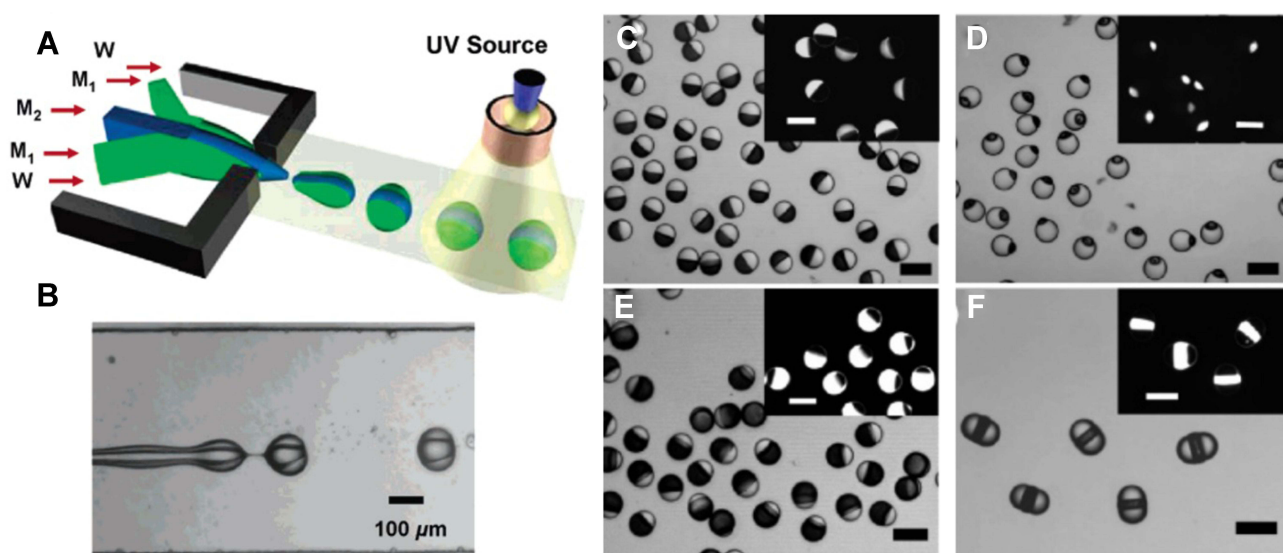

Figure 3 Microfluidic device that uses immiscible co-flowing streams to generate Janus and ternary microparticles. (**A**) Device schematic, where M1 is methacryloxypropyl dimethylsiloxane, M2 is a mixture of pentaerythritol triacrylate, poly(ethylene glycol) diacrylate and acrylic acid, and W is aqueous SDS (sodium dodecyl sulfate) solution. (**B**) Droplet generation from co-flowing streams, (**C–F**) optical and fluorescent (inset) microscopy images of the synthesized particles with varying ratios of monomers. (parts of two figures were merged from the original paper). Adapted with permission from Nie Z, Li W, Seo M, et al. Janus and ternary particles generated by microfluidic synthesis: design, synthesis, and self-assembly. *J Am Chem Soc.* 2006;128(29):9408–9412 . Copyright (2006)American Chemical Society.[54]

A mixture of a hydrophilic monomer and a hydrophobic monomer was used as the dispersed phase. Due to the surface modification of the microchannel, the hydrophilic monomer flowed along the hydrophilic part of the microchannel and the hydrophobic monomer flowed along the hydrophobic part of the microchannel. The two parallel streams were sheared into droplets followed by UV exposure to form amphiphilic particles.[57] Recently, Haney et al reported the synthesis of hydrophobic-hydrophilic Janus particles as a stabilizing agent in emulsions that could be used as a potential replacement for conventional surfactants.[58]

Phase Separation

Phase separation provides an excellent pathway for Janus particle synthesis. It relies on the fact that the reaction of monomers to energy absorption depends on their chemistry.[59] This method does not require precise control of flow parameters, making it a simpler approach than the co-flowing technique which depends on the precision of the flow parameters to maintain the interface that separates the two halves of the Janus particles. Shah et al reported one of the first studies on the phase separation method where they synthesized Janus microparticles with one side made of a hydrogel and the other side made primarily of aggregated colloidal nanoparticles. They used a two-step phase separation method consisting of heat-induced shrinkage and accumulation of microgels to one hemisphere, and UV polymerization of an acrylamide monomer in the other hemisphere.[60] The utilized microgels were cationic, so anionic magnetic beads accumulated in the same hemisphere and rendered the spherical particles magnetically anisotropic. Lone et al reported fabrication of Janus particles with a protruding head to give physical anisotropy using UV-directed phase separation. Firstly, droplets of an aqueous phase, consisting of a thermosensitive and a photosensitive compound, were formed in a flow-focusing geometry using hexadecane as the continuous phase. The UV-directed phase separation was achieved in a two-step procedure where a light-sensitive compound (spironaphthoxazine) present in each droplet pushed the other water-based thermosensitive monomer (Poly(N-isopropylacrylamide)) to the tip of the spherical droplet upon UV exposure as a result of zwitterionic pair effect. This led the way for the photoinitiator from the continuous phase to diffuse into the tip and initiate polymerization and form the anisotropic Janus particle.[61] Kim et al reported a novel technique that took advantage of the difference in the rates of phase separation and UV polymerization between two hemispheres to synthesize asymmetric porous Janus particles. They generated droplets of the dispersed phase composed of a nematic liquid crystal, that causes the polarization of light waves, mixed with a polymer. The generated droplets were then collected and exposed to UV radiation. It was observed that the droplet hemisphere directly facing UV radiation swelled (and wrinkled when dried), while the other hemisphere remained smooth making the particle asymmetrically porous.[62] Li et al altered the contents of the dispersed phase from an organochloride compound (dichloromethane) to an organic compound (dimethyl carbonate) for phase separation-based Janus particle synthesis. They concluded that by changing the nature of the dispersed phase from an organochloride to an organic fluid, a morphology transition from core-shell microcapsule to Janus could be achieved.[63] Another study based on phase separation was reported by Jeong et al where a solution of incompatible monomers was used to form anisotropic particles. The droplet phase was a mixture of three polymers, two of which were incompatible with the third one. As heat was provided, the solvent in the droplets evaporated and the incompatible polymers separated into two compartments giving the particle its Janus characteristic.[64] Ekanem et al reported the synthesis of anisotropic particles containing patches on one part of the particles. The extent of patches was found to depend on emulsion formulation, droplet size, and synthesis route. They concluded that smaller droplets resulted in patchy particles and larger droplets contained no patches. The difference in the resulting morphology was attributed to shorter solidification time required for smaller droplets which prevented the complete phase separation of polymers present in each droplet.[65]

Wang et al synthesized amphiphilic polymer particles having magnetic anisotropy by an off-chip magnetically driven phase separation method.[66] Sun et al utilized a simple flow-focusing droplet generator coupled with a downstream serpentine channel to synthesize novel Janus particles having separate lipid (triglyceride type) and polymeric (poly(lactic-co-glycolic acid)) compartments. The morphology of the particles was easily tuned from Janus-patchy to triple, quadruple and core-shell type by varying the amount and type of surfactant incorporated into the dispersed phase.[67] Ghosh et al reported the synthesis of snowman-like Janus hydrogel particles by solvent evaporation-based phase separation.[68] Xia et al used the solvent loss-based phase separation method to demonstrate how the density of suspended particles could lead to phase separation and shape alterations in Janus particles. They demonstrated that low-density microparticles led to more spherical, and high-density nanoparticles led to flattened particle shapes.[69] Utilizing phase separation method based on solvent loss, Ren et al synthesized crescent-shaped Janus particles
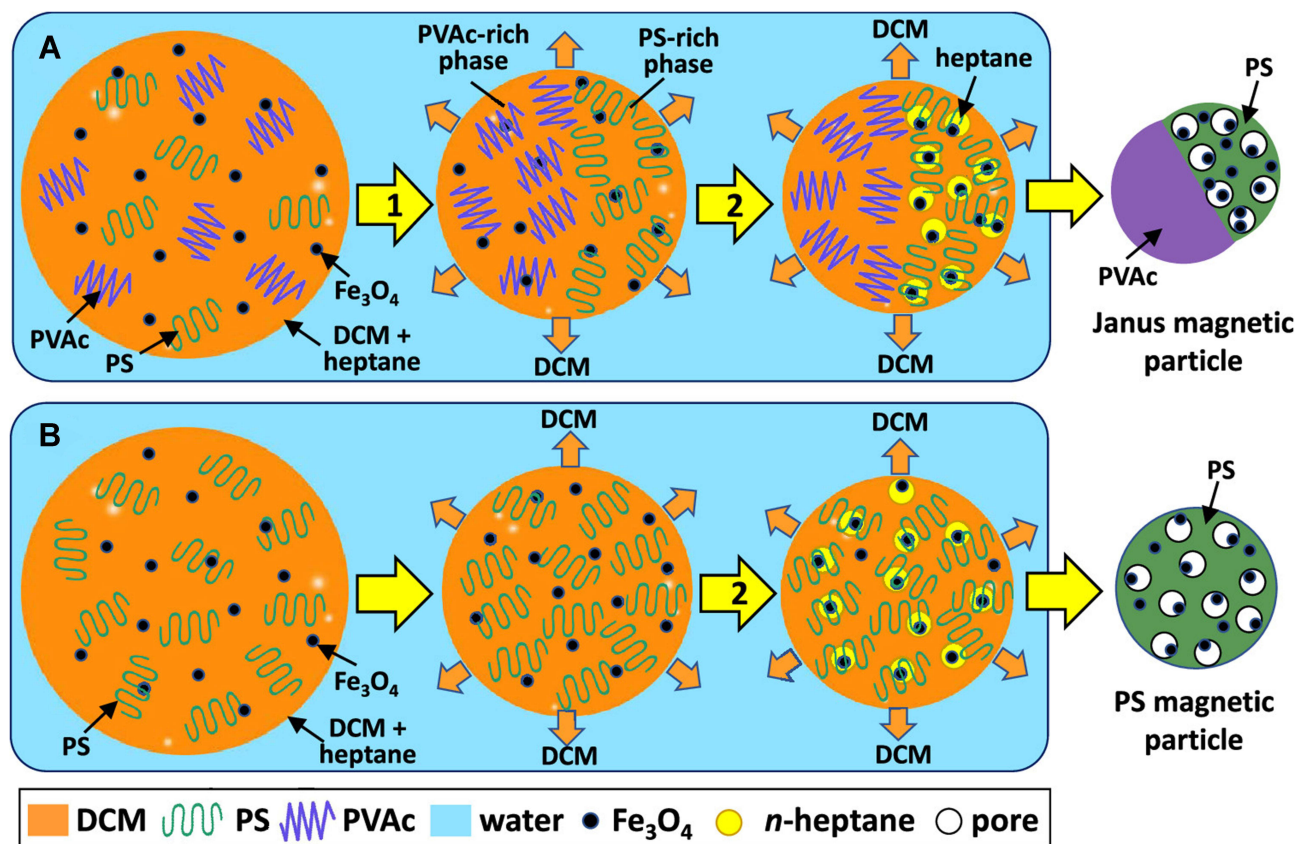
Figure 4 (**A**) Schematic showing the formation of magnetically anisotropic and highly porous polymeric particles due to the two step phase separation between polystyrene and poly(vinyl acetate). (**B**) Illustration of the two step synthesis of highly porous isotropic magnetic polymer particles. DCM: dichloromethane; PS: polystyrene; PVAc: poly (vinyl acetate), Fe₃O₄: magnetic nanoparticles. Reprinted with permission from Al Nuumani R, Smoukov SK, Bolognesi G, et al. Highly porous magnetic Janus microparticles with asymmetric surface topology. *Langmuir.* 2020;36(42):12702–12711. Copyright 2020 American Chemical Society.[70]

decorated with manganese oxide nanoparticles on the concave surface and magnetic nanoparticles on the convex surface for water decontamination applications.[26] Recently, Al Nuumani et al successfully synthesized anisotropic magnetic Janus particles to be porous on one hemisphere and non-porous on the other one using the process shown in Figure 4.[70] This was achieved by a two-step solvent evaporation-based phase separation. In the first step, the phase separation of thermodynamically incompatible monomers caused hemispherical partitioning, and in the second step the phase separation of dichloromethane and heptane led to the formation of pores on one hemisphere. In a more recent work, Lan et al utilized a phase separation technique based on UV exposure coupled with solvent evaporation to synthesize snowman-shaped amphiphilic Janus particles using materials derived from plants that could be potentially used as environment-friendly replacements for microplastics. In contrast to the previous research reports, this work not only presented a novel approach to synthesize amphiphilic Janus particles but also demonstrated a practical solution to address the low throughput drawback of microfluidic platforms by using 10,260 parallel microdroplet generators in a single silicon-and-glass microfluidic device to scale up the synthesis.[71]

Double Emulsion

In the double emulsion method, droplets of one phase (oil or aqueous) encapsulate the droplets of the other phase to generate encapsulated droplets within a microfluidic channel. This is achieved by selective treatment of the microfluidic channels to form hydrophobic and hydrophilic regions within the same device. Chen et al reported the formation of non-spherical Janus particles using this approach as shown in Figure 5.[72] During transportation of droplets inside the channel, the inner droplet was pushed towards the back side of the encapsulating droplet due to hydrodynamic forces and density difference between the two droplets. The double emulsion droplets were then cured with UV exposure to freeze their Janus configuration. Chen et al used this approach to synthesize anisotropic magnetic Janus particles by incorporating magnetic nanoparticles into the inner droplet
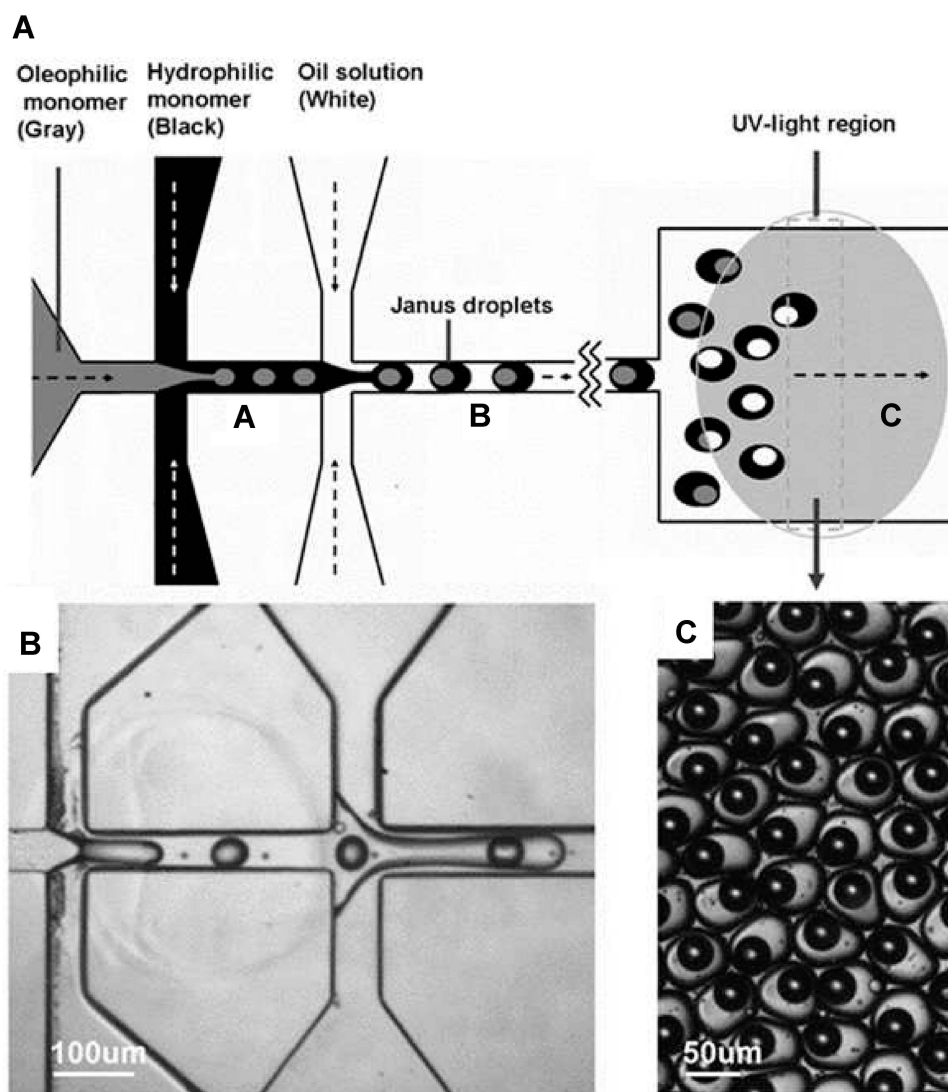
Figure 5 (**A**) Schematic of a double emulsion microfluidic device and droplets formed with one core. (**B**) Optical image of double emulsion Janus droplet formation in a PDMS device. (**C**) Optical image of the collection reservoir where the double emulsion droplets are collected and exposed to UV radiation to initiate polymerization. Reprinted with permission from Chen CH, Shah RK, Abate AR, et al. Janus particles templated from double emulsion droplets generated using microfluidics. *Langmuir.* 2009;25(8):4320–4323. Copyright (2009) American Chemical Society.[72]

phase.[73] Thiele et al further advanced this methodology by adding a third consecutive droplet generation unit to provide extra microgel spheres which acted as a support to prevent shape change during the UV exposure.[74] Using this approach, non-spherical snowman-shaped particles having internally hydrophilic or hydrophobic lobes and an outer hydrophilic shell could be successfully synthesized. These Janus particles were proposed to be a potential replacement for conventional surfactants as an emulsion stabilizer.

In the case of double emulsion method, over-reliance on oil-in-water emulsions has been a major hurdle in the ability of the obtained particles to encapsulate biomolecules. For this reason, there is a lot of attention towards utilizing multiple all-aqueous emulsions to synthesize Janus particles.[75] In a recent study, Dumas et al demonstrated how water-in-water emulsions could be stabilized by adsorbing chitosan-grafted lipid nanocapsules at the interface between the two aqueous phases. If such a method could be utilized to synthesize Janus particles, not only would it allow encapsulation of biomolecules it would also open new frontiers for drug delivery applications.[76]

Electrohydrodynamic Co-Jetting

Electrohydrodynamic (EHD) co-jetting is a technique in which co-flowing streams of fluids are pumped in air across an electric field to induce electrified jetting to obtain anisotropic particles. Roh et al were among the first scientists to report the synthesis of Janus particles using this method.[77] They studied how changes in the interfacial tension values between the co-flowing fluids caused changes in the particle shapes to obtain peanut, snowman, and spindle-like particle morphologies. Their results showed that these particles exhibited excellent anisotropy and no cross-contamination of payloads occurred between the spherical halves. In another work, Hwang et al reported the synthesis of spherical Janus nanoparticles consisting of two different types of polymer hemispheres for use in controlled release of multiple drugs.[78] The synthesized Janus particles demonstrated selective, pH-dependent degradation of each hemispherical compartment. Rahmani et al conducted another study where 100 nm sized Janus particles were obtained by EHD co-jetting by altering process parameters, including polymer composition, polymer concentration and type of surfactant.[79] In a recent work, Feng et al reported the synthesis of drug-loaded magnetic Janus particles using EHD co-jetting method. The particles comprised three compartments that possessed different functionalities, namely magnetic nanoparticles for targeting, dyes for fluorescent tracking, and drugs for killing cancer cells. According to their findings, these multicompartmental particles were more efficient in targeting and killing cancer cells than conventional techniques.[12]

Miscellaneous Techniques

Aside from the techniques discussed above, there are other methodologies for the microfluidic production of anisotropic particles. Lu et al reported the synthesis of dumbbell-shaped anisotropic Janus particles having magnetic properties for micromixing applications. Janus particles were synthesized by the coalescence of two adjacent droplets as shown in Figure 6. One droplet contained chitosan and the other contained magnetic nanoparticles in chitosan.[80] As the droplets came into contact, glutaraldehyde was introduced into the microchannel which initiated the cross-linking of chitosan resulting in dumbbell-shaped chitosan particles. Shang et al reported the fabrication of Janus particles composed of iron oxide (Fe_3O_4) and silicon dioxide (SiO_2) in distinct hemispheres using droplets as particle templates. Droplets were cured
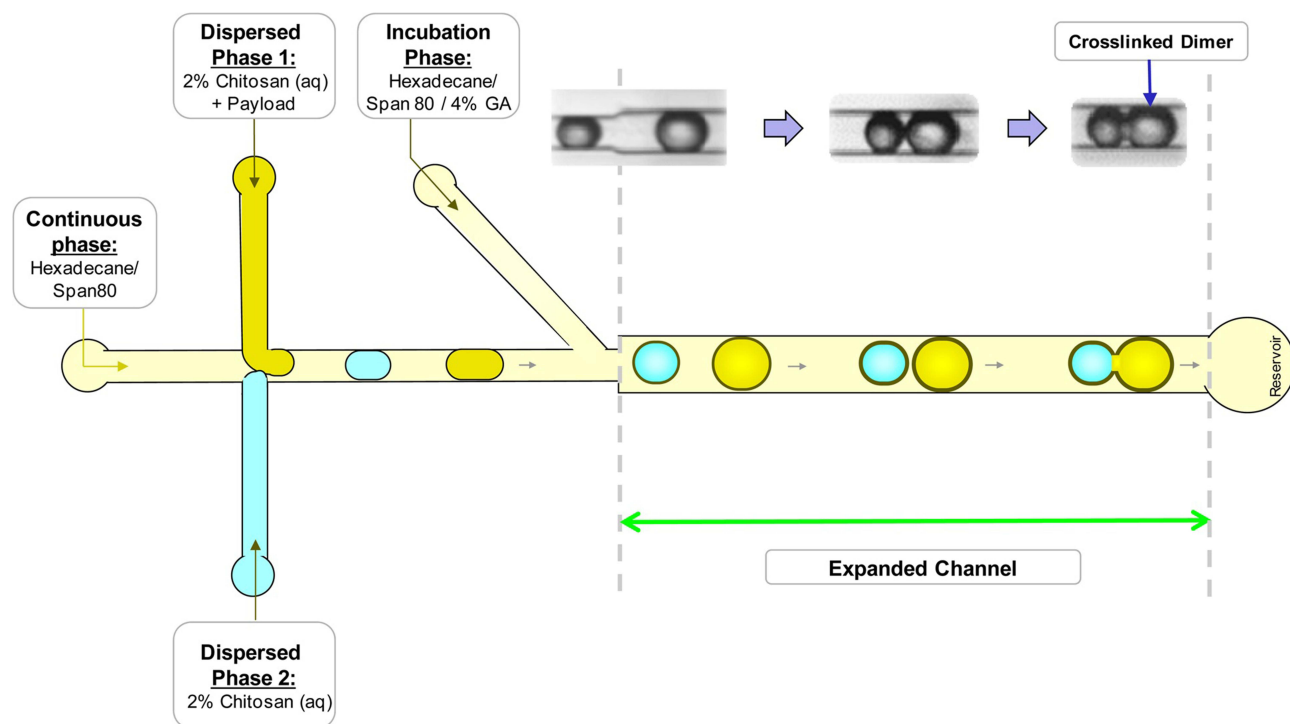

Figure 6 Schematic of the microfluidic device used to synthesize dimer like Janus particles. Reprinted with permission from Lu AX, Jiang K, DeVoe DL, et al. Microfluidic assembly of Janus-like dimer capsules. *Langmuir*. 2013;29(44):13624–13629. Copyright (2013) American Chemical Society.[80]

off-chip in the presence of a magnetic field which resulted in anisotropic Janus particles.[81] Using a similar approach, Chen et al reported the production of Fe_3O_4 and TiO_2 Janus particles using branched polymers by off-chip magnetic and gravitational force-based separation, followed by thermal curing.[82] Torii et al fabricated anisotropic magnetic Janus particles by an off-chip gelation process initiated by diffusion of ions from the droplet to an agarose gel plate.[83] Although effective, off-chip processing is not desirable in microfluidic-based particle synthesis. Varma et al reported the synthesis of anisotropic magnetic Janus particles for protein detection by on-chip magnetic force-based separation, followed by UV polymerization.[84] In a more recent work, Wang et al fabricated Janus nanostructures composed of gold nanorods and silver, by a simple microfluidic droplet-based reactor and serpentine mixer.[85] They demonstrated the use of these Janus structures as nanosensors for the detection of mercury ions. Such particles could be commercially utilized for the detection of mercury in drinking water to avoid harmful effects of mercury ingestion. Recently, Li et al reported a novel method to synthesize Janus colloidal photonic crystals for potential use on a flexible display. The shortcoming in the earlier conventional methods, for example in the method reported by Yu et al,[38] was that the colloidal photonic crystals were formed inside a microfluidic chip and therefore, needed to be transferred onto the grooves on the flexible display by a complex and painstaking process. To address this issue, Li et al designed a system that combined a microfluidic droplet generator with an automatic dispensing printing system to synthesize and print Janus colloidal photonic crystals on a flexible display. The vertical microfluidic droplet generator formed droplets from two sources. These droplets came into proximity of each other and merged to form a Janus structure due to the interfacial tension between the two phases, and were dispensed onto a flexible display. This eliminated the tedious process of transferring the synthesized colloidal structures from a microfluidic device onto a substrate.[86]

Conclusion

In this review, microfluidic-based synthesis routes for Janus particles have been discussed including co-flowing streams method, phase separation method and double emulsion method among others. While these conventional microfluidic-based synthesis routes enable the fabrication of monodisperse Janus particles having complex functionalities, they exhibit certain shortcomings, such as the need for similar viscosities for dispersed phases in the co-flowing streams, precise control over fluid flow rates for the double-emulsion method, and difficulty in achieving equilibrium in phase separation processes due to constantly changing physical properties of fluids throughout the process. Microfluidic-based techniques provide a superior pathway for the synthesis of Janus particles as compared to conventional batch synthesis techniques due to their ability to synthesize monodisperse particles using a small volume of reagent typically on a single chip. Recent advances in microfluidic-based techniques for Janus particle synthesis provide the ability to fabricate a wide variety of particle shapes using non-hazardous, biogenic materials in the nanometer regime. This is of utmost importance for the potential use of these anisotropic particles in several applications critical to human life, ie removal of contaminants (metal traces, bacteria, microplastics, oil, etc) from water, and detection of bacteria and toxins. On the other hand, for applications requiring a large number of particles, scaling up of production is necessary and is still a challenge for microfluidic-based methods. Furthermore, conventional microfluidic devices are fabricated using specialized equipment which makes their manufacturing expensive. In addition, microfluidic platforms require pumps and external valves to operate, which makes the device prone to leakage. Nevertheless, several parallelization techniques were utilized in recent reports that allowed the production of monodisperse droplets from multiple nozzles at a time, at a generation frequency of several kHz. Moreover, many potential replacements to conventional microfluidics platforms have been introduced, ie, paper-based microfluidics which are easy to manufacture and eliminate the need for pumps and external valves. To conclude, Janus particles have the potential to contribute massively to some of human kinds' technological challenges, and although microfluidic-based techniques have certain limitations, the recent advances in the field of microfluidics leave us optimistic about the future prospects for the use of these methods for Janus particle synthesis.

Acknowledgments

Disclosure

The authors report no conflicts of interest in this work.

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