

# Polymer Colloids: Moving beyond Spherical Particles

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**Abstract:** When thinking about colloidal particles, the first image that comes into mind is that of tiny little polystyrene spheres with a narrow size distribution. While spherical polymer colloids are one of the workhorses of colloid science, scientists have been working on the development of progressively advanced strategies to move beyond particles with spherical shapes, and prepared polymer colloids with more complex morphologies. This short review aims at providing a summary of these developments, focusing primarily on methods applicable to submicron particles, with an eye towards their applications and some discussion about advantages and drawbacks of the various approaches.

**Keywords:** Emulsion polymerization · Non-spherical particles · Polymer colloids · Self-assembly



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## 1. Introduction

Polymer colloids are one of the most well studied, abundantly researched, and best understood systems in colloidal science.<sup>[1]</sup> Their application range is very wide and includes paints, coatings, production of bulk polymer commodities, drug delivery vehicles, and packing materials in chromatographic columns, just to mention some of the most important commercial uses.<sup>[2]</sup> Polymer colloids have also greatly contributed to the understanding of the fundamentals of colloidal science, as they have been used as large size equivalents of atoms, and have helped physicists to expand the theory of phase transitions. They also contributed to reach a better understanding of phenomena such as crystallization and

glass transition, and have therefore greatly contributed to the development of soft matter science.<sup>[3]</sup> Thanks to the development of simple and reliable synthesis strategies, mostly based on emulsion, dispersion or precipitation free-radical polymerizations, their preparation, for standard polymers such as polystyrene (PS) and polyacrylates, is easy, standardized, their size range can be controlled over several orders of magnitudes, from about 10 nm up to tens of micrometers, and they can be produced with extremely narrow size distributions, hardly matched by any other particles made of inorganic materials.<sup>[4]</sup> Not surprisingly, PS colloids are the particles used as standards for testing and calibration of most particle size measuring devices. The development of emulsion polymerization is one of the reasons of the success of polymer colloids. It is one of the methods of choice for the industrial production of commodity polymers, such as polyvinyl chloride, various fluorinated polymers, several acrylates and various types of rubbers thanks to its unique control of reaction conditions, even when a particulate dispersion is not the final product.<sup>[4d,e]</sup>

Advances in polymer chemistry and in the synthesis of functional monomers have allowed the incorporation of progressively more sophisticated functional groups inside polymer colloids, which have been used to either impart unique properties to particles (*e.g.* responsiveness to stimuli, controlled porosity, and development of complex internal architectures), the incorporation of dyes and especially to alter their surface chemistry. This has led to the development of a wide range of surface modification techniques, which allow colloidal scientists to fine tune the stability of the particles, and to control their interactions with the environment.<sup>[2b,4e]</sup>

While the control of composition, size and internal structure of polymer colloids has led to exciting developments, there is one additional crucial parameter that is much more difficult to control: the shape of polymer colloids. This observation is a simple consequence of the syntheses used to prepare polymer colloids. In spite of the enormous benefits that emulsion and precipitation-based techniques offer, they almost inevitably lead to spherical particles, because this shape is the one that minimizes the surface, and consequently the interfacial energy, of a particle with a given volume. Moving beyond a spherical shape means fighting against thermodynamics, and it is not surprising that this is a difficult battle.

Before dwelling on how and to which extent a control of the particle shape can be achieved, it is important to understand why and when a control of shape is desirable. A first example comes from the field of biomedicine. Spherical (nano)particles have

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been abundantly investigated for drug delivery applications.<sup>[5]</sup> It is well established that the successful development of a drug delivery platform heavily relies on a few crucial aspects: their surface functionality, which determines their stability in a challenging environment and is the part that comes in contact with the biological medium, thus playing the most crucial role; the size of the particles, which determines the uptake mechanism and the fate of the particles, and the shape. The latter has proved to affect how particles interact with cells, and also the transportation mechanism inside, for example, blood vessels. The group of Mitragotri<sup>[5,6]</sup> has pioneered these investigations, and shown how highly elongated particles with the same volume, with the same surface properties and made of the same material as their spherical counterpart interact very differently with cells.

A second research area that is growing in importance is the development of particles capable of self-propulsion, often referred to as microswimmers.<sup>[7]</sup> Inspired by microorganisms, these particles can be considered as a primitive form of micromachines, and hold promise for various applications, especially in the biomedical fields. It is clear that, in order to impart particles with a self-propelling ability, the spherical symmetry has to be broken, either by providing an asymmetric surface functionalization, or directly by creating non-spherical particles, with a portion dedicated to self-propelling.<sup>[7a]</sup> Because of the flexibility offered by polymers in the design of devices to be used in medicine, the development of non-spherical polymer particles as parts of microswimmers is a very active field of research.

Spherical particles have also been investigated in the field of material science as building blocks for self-assembly.<sup>[8]</sup> Colloidal crystals are one of the only examples of well-defined superstructures formed starting from spherical particles, and are the macroscopic equivalent of crystalline solids made of atoms.<sup>[9]</sup> These colloidal crystals have been investigated for optical applications, because when the particles forming them are in the size range of the wavelength of visible light, they can selectively reflect light with a wavelength that depends on their spacing, leading to structural coloration.<sup>[8b,c,10]</sup> However, while atoms have the ability to form directional bonds, which lead to the formation of a variety of crystalline structures, the spherically symmetric interaction potential of spherical particles leads almost inevitably to the formation of crystals with face-centered cubic structures. It has, however, been shown recently by the group of Pine that more interesting colloidal crystals can be formed, such as colloidal crystals with diamond-like structure, when particles can crystallize with only four neighbors.<sup>[11]</sup> This has been achieved by working with non-spherical particles with tetrahedral geometry. Accessing a broader variety of crystalline structures opens up new possibilities in the field of optical materials.

A simpler consideration can be made by extending the analogy between spherical particles and atoms. It is clear that the wealth of structures accessible by atoms is due to their ability to form molecules, which almost never have a spherical shape. The precise geometry of molecules and their ability to form well-defined directional bonds is the key that leads to the formation of highly complex structures.<sup>[12]</sup> It is therefore natural to develop strategies that would allow to control the shape and, when possible, the functionality of polymer colloids, beyond the standard spherical shape. In the following section a brief overview of the methods developed in the literature to control the shape of polymer colloids is provided, together with a critical analysis of their advantages and drawbacks. The review will only consider pure polymer colloids, not polymer micelles, and will only cover methods not involving the use of inorganic particles as templating agents.

## 2. Synthesis of Non-spherical Polymer Particles

Inorganic nanoparticles can often be prepared with a variety of shapes, using the natural crystalline nature of their atomic

structure, which leads to the presence of facets.<sup>[14]</sup> Exploiting the natural difference in growth rates of these facets, or using ligands with a preferential binding affinity for a given crystalline facet, are two of the most common strategies used to control the shape of inorganic particles. The intrinsic amorphous structure of polymer particles prevents the exploitation of such a strategy. There are several strategies used to create non-spherical polymer particles, and Fig. 1 shows a few examples of those particles, the synthesis of which is discussed in this review.

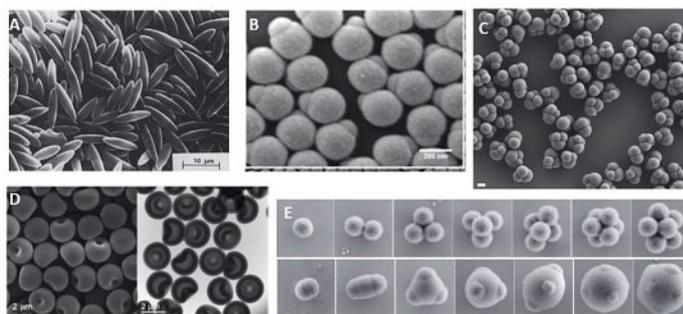
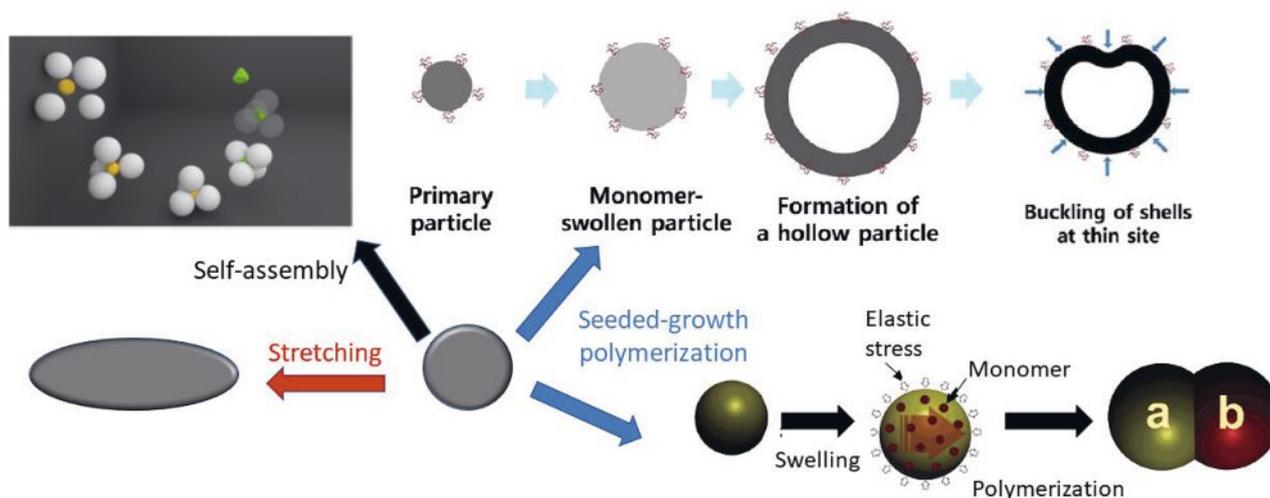


Fig. 1. A series of SEM images of a variety of non-spherical polymer particles, discussed in this article. All reprinted with permission. A) Ellipsoidal PS particles,<sup>[13]</sup> B) PS dumbbells,<sup>[14]</sup> C) Tetrahedral particles made of PS and 3-(trimethoxysilyl) propyl methacrylate,<sup>[15]</sup> D) SEM and TEM images of dimpled PS particles,<sup>[16]</sup> E) Colloidal clusters and corresponding patchy particles, made from an increasing number of spherical PS colloids.<sup>[17]</sup>

We will focus our attention primarily on methods that work in bulk, and which are applicable to particles in the sub-micron to micron size range. The variety of approaches developed can be grouped together in three main groups, all of which start from spherical particles: mechanical deformation, self-assembly and seeded growth polymerization. Scheme 1 shows graphically this classification. Mechanical deformation of the particles is one of the oldest methods developed to change the shape of spherical particles into ellipsoidal particles, while keeping their monodispersity.<sup>[13]</sup> The idea behind this method, first applied to polystyrene colloids, consists of immobilizing spherical non-crosslinked colloids in a polyvinyl alcohol (PVA) film. Upon solidification of the matrix, the solid material is heated up above the glass transition temperature of the polymer particles, followed by a deformation step in which the PVA film is mechanically stretched in either one direction, or even in two directions. Upon quenching the temperature below the glass transition temperature of the polymer, the PVA matrix is removed and the particles redispersed in an aqueous media. Fig. 1A and 1B show SEM pictures of stretched PS particles. A stretching along a single direction leads to prolate spheroidal particles, with an aspect ratio that is tunable by the extent of stretching. A biaxial stretching leads instead to oblate spheroidal particles. The method has been applied to other polymers beyond polystyrene, such as polylactic acid, leading to biocompatible particles, in order to investigate the shape effect on cellular uptake and interaction.<sup>[6b]</sup> Simple to apply, and leading to highly monodisperse non-spherical particles, the deformation of particles above their glass transition temperature has been for a long time one of the only strategies used to prepare non spherical polymer particles. Its main drawback is the yield, which is very low, due to the difficulty of scaling this approach up. Furthermore, the redissolution of the PVA after deformation is a long and laborious process.



Scheme 1. Graphical classification of the main methods presented in the literature, and discussed in this work, for the preparation of non-spherical polymer colloids. Adapted and reprinted with permission from references (from left to right): refs [18], [16] and [19].

The second class of methods that has been exploited to prepare non-spherical polymer colloids is self-assembly. It is well known that aqueous suspensions of colloidal particles are often stabilized by charges. This electrostatic stabilization can be regulated by controlling the ionic strength of the solution, which can be easily achieved through the addition of electrolytes.<sup>[1]</sup> When these electrostatic interactions are screened, the attractive Van der Waals interactions drive the self-assembly of particles. Without any precaution, this process leads to the formation of highly disordered aggregates, with fractal morphology.<sup>[20]</sup> The group of Velegol has however managed to stop the process at the very first stage of the aggregation, which leads to the formation of dumbbells, *i.e.* two particles connected together, which have been partially fused in order to permanently fix their structure.<sup>[21]</sup> In order to obtain more complex geometries, some clever strategies have been devised. The group of Pine has developed a very interesting method, in which crosslinked polystyrene particles have been dispersed in toluene, and the dispersion has been emulsified in water, leading to an oil-in-water emulsion.<sup>[22]</sup> Upon removal of toluene by evaporation, the capillary forces led to the formation of well-defined clusters of spheres, containing 2–12 particles, with a clearly defined packing. Fractionation of these clusters by differential gradient centrifugation has allowed the authors to obtain pure fractions of the individual clusters. The process has been further modified by adding monomers to the cluster and polymerize it, leading to patchy particles with a well-defined number of patches.<sup>[17]</sup> Functionalization of those patches with DNA allowed the preparation of colloidal molecules. More recent work by Sacanna's group has introduced the concept of colloidal fusion as a clever strategy to prepare polymer particles with well-defined shapes.<sup>[18]</sup> The idea is to use heteroaggregation, *i.e.* aggregation among negatively-charged droplets and oppositely charged particles, where the particles are in large excess with respect to the droplets, and the size ratio between particles and droplets is carefully chosen. Polymer bridging flocculation has also been used instead of heteroaggregation. The aggregation between one droplet and particles leads to the formation of clusters with well-defined structures, because the particles can move once bound to the droplet, thanks to the liquid nature of the latter. The excess of particles provides optimal conditions for the formation of clusters with defined geometrical configurations of particles, which position themselves so as to minimize their repulsion. The number of particles that can bind to a droplet depends on the size ratio between particles and droplets and has been tuned from three to six. When the liquid droplet was made of a monomer, such as 3-(trimethoxysilyl) propyl methacrylate (TMP), polymerization

has been used to fix the structure. Furthermore, the addition of a solvent that partially solubilizes the particles can lead to a partial fusion of the cluster, resulting in patchy particles with a tunable morphology.<sup>[11]</sup> Aggregation has also been used by Kraft and coworkers, who prepared crosslinked polymer particles, swelled them with a monomer, and used the liquid protrusion formed by the monomer being exuded by the particles to connect particles together *via* the liquid.<sup>[23]</sup> Upon polymerization to fix the structure, dumbbells, trimers and larger particles with a geometrically controlled number of lobes have been prepared. A similar procedure has also been applied to prepare multilobed particles with an unequal surface roughness on the various lobes.<sup>[24]</sup> Self-assembly is a powerful strategy, with the potential to prepare particles with a highly sophisticated shape and morphology, and with controlled composition. Its main drawback is that, once again, it is difficult to scale up, because self-assembly can be optimally controlled only under dilute conditions, and also because some separation or size sorting step is always required, which often limits the yield of the overall process.

The third method is based on the application of multiple swelling and polymerization steps, starting from well-defined spherical polymer particles. The method has been reported for the first time by El-Aasser and coworkers more than thirty years ago.<sup>[25]</sup> They noticed that, when swelling a crosslinked polymer particle with a monomer, this does not result in any core shell structure, but rather in the formation of a new lobe, which leads to a dumbbell particle. The reason is that a crosslinked particle accumulates too much mechanical stress when swollen with a monomer, and the stretched network reacts by inducing a phase separation of the added monomer, which forms a new lobe that can be polymerized. This effect has been systematically investigated as a method to produce non-spherical particles almost two decades later by the Weitz group.<sup>[19,26]</sup> They first prepared monodisperse polystyrene particles, followed by a swelling step aiming at introducing a controlled extent of crosslinking. A subsequent additional swelling and polymerization step with styrene leads to the formation of dumbbells. They used these particles as particle-surfactants for the stabilization of oil-in-water Pickering emulsions.<sup>[26b]</sup> The process has been extended to prepare trimers, and control the position and growth of the third lobe by fine tuning the crosslinking.<sup>[26a]</sup> Several authors have extended the method to smaller particles, by playing with the coating of the original particles, which leads to a reduction of the interfacial tension necessary to develop a new lobe.<sup>[14,27,28]</sup> TMP is one of the monomers often combined with styrene, to achieve this result. Honciuc *et al.* have extended the method to prepare trimer particles with three lobes having a differ-

ent composition,<sup>[29]</sup> while Weck *et al.* have managed the preparation of tetrahedral particles with chiral properties.<sup>[15]</sup>

Our group has also been actively working in the field, first by producing dumbbell particles and using them to make asymmetrically functionalized silica nanobowls,<sup>[27]</sup> and currently by aiming at developing simpler and more effective methods to control the shape of polymer particles. Some of the particles that we have been able to prepare are showcased in Fig. 2. The procedure used starts from a polystyrene seed, prepared by emulsion polymerization, which is then swollen with a mixture of styrene and TMP. The latter, depending on the pH of the solution, hydrolyzes and changes substantially the surface properties of the seed. Upon further swelling, dumbbells with various morphologies have been prepared, with the possibility to control the roughness of the second lobe. The preparation of a third lobe, with either the same composition, or with the use of a different monomer has also been achieved.

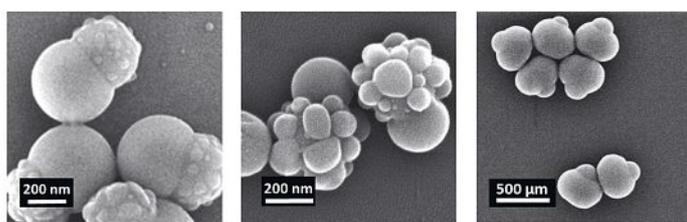


Fig. 2. SEM images of non-spherical polymer particles produced in the Lattuada group, using an optimized version of the seed-growth polymerization method.<sup>[27]</sup> Left and center: PS dumbbells with controlled surface roughness on one lobe. Right: PS-PMMA trimer, with two lateral lobes made of PS, while the third lobe of polymethyl methacrylate (PMMA) is located in between the PS lobes in an equilateral triangular configuration.

A special group of particles, commonly referred to dimpled particles, which consist of spherical particles with one well-defined cavity on their surface, have also been prepared by exploiting either a swelling-polymerization step, or the addition and then the removal of a solvent.<sup>[30]</sup> In general, the formation of dimpled particles involves the preparation of colloids with a crosslinked shell, which tends to buckle and partially collapse when the particles are exposed to physical conditions that change the density or composition of their core. For example, when particles with a crosslinked shell are swollen with solvents that can solubilize their core, upon solvent removal their shell can collapse, leading to a well-defined cavity.<sup>[31]</sup> Similar results can be obtained by using protocols in which monomers and crosslinkers are slowly and continuously added during the particle synthesis, leading to preferential consumption of the latter, which is usually chemically more reactive, and forms a thin crosslinked layer on the surface.<sup>[30]</sup> A very versatile method involves first the coating of spherical particles with glucose, which, upon caramelization at around 200 °C, forms a rigid shell around the particle.<sup>[32]</sup> Exposure of these particles to an alcohol, under pressure and again at the same temperature as in the previous step, leads to the formation of a well-defined dimple on the particle surface. Dimpled particles have been used in interesting lock-and-key experiments, where spherical particles would accommodate preferentially inside the cavity driven by depletion interactions created by soluble polymers dispersed in solution.<sup>[33]</sup> More recently our group has devised a procedure to control the shape of particles, leading to dimpled particles, or hemispheres, or more complex geometry, by using a modification of the activated swelling method pioneered by Ugelstad.<sup>[34]</sup> It turns out that, starting from polystyrene seeds, and by swelling them with an acrylate (or a mixture of them) and a crosslinker, in the presence of inhibitors for the polymerization, the morphology of the particles

can be controlled, because the presence of inhibitors acts strongly on monomers but less so on the crosslinkers. Therefore, a rigid polymer shell is formed around the growing particles, and a mechanical instability is once more responsible for the deformation of the particles. The interesting feature of this method is that, not only the shape of the particle is controlled, but their composition as well, such that dimpled Janus particles have been successfully prepared. This third group of methods permits in theory to avoid some of the problems of the first two strategies, because emulsion polymerization methods allow the preparation of concentrated suspensions of particles, and are easily scalable. Even swelling and repolymerization steps, although they are not easily working with very high concentrations of particles, can still be applied to suspensions containing a few weight percent of particles, which is usually more than what can be achieved with all the other methods previously discussed. However, the reproducibility of the results is not always guaranteed, because most of the methods rely upon swelling steps, which can compromise the colloidal stability of particles. Therefore, careful control of all the factors affecting the colloidal stability of particles, such as ionic strength, pH, and addition of surfactants, is required, and small variations in one of these parameters can lead to failures.

A few other methods are worth mentioning, which are not classified as ‘bulk’ methods, but which have nonetheless been proposed, and in some cases, commercialized. The first example is the adaptation of lithography to the preparation of polymer particles for biological applications. With the ever-growing improvement of lithographic methods for electronics, their applications in soft matter have been explored. The most successful example is a commercialized technology under the trade name PRINT (Particle Replication In Non-Wetting Templates).<sup>[35]</sup> The company commercializing it has already brought to the market one product used in the treatment of a new formulation for a vasodilator used in the treatment of pulmonary arterial hypertension.<sup>[36]</sup> Another example, primarily applicable to the preparation of very large polymer particles (~tens of micrometers), is a method based on microfluidics called stop-flow lithography, which has been shown to be able to prepare particles with complex architectures, such as barcode particles.<sup>[37]</sup> Finally, the constantly improving 3D printing methods have also been used for the preparation of polymer particles with complex geometries, and for microswimmers, still in a size range of about 10 micrometers.<sup>[38]</sup>

### 3. Conclusions

In all the standard methods to synthesize polymer colloids, thermodynamics drives, almost always, towards spherical particles. These particles have allowed scientists to make much progress in the fundamental understanding of the behavior of colloids suspensions, in optimizing synthesis, functionalization methods, and to develop many successful commercial products based on these materials. Attempting to go beyond what thermodynamic dictates requires a plethora of new techniques, ideas, and protocols, that can further expand the range of applications of polymer particles. However, many hurdles are still ahead, especially when dealing with scaleup and reproducibility. With new developments in sight, such as the micro- and nanorobotics, it is clear that polymer particles can play a crucial role in providing building blocks, functional units, *etc.*, and this alone justifies the many research efforts in this area. Even though the sphere is ‘the most perfect shape’, going beyond it is worth while, even at the cost of losing some ‘perfection’.

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