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Recent Advances in the Emulsion Solvent Evaporation Technique for the Preparation of Nanoparticles and Nanocapsules

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Abstract The emulsion solvent evaporation technique is a method for preparing nanoparticles and nanocapsules that are particularly adapted for applications requiring materials with high purity and low toxicity, such as for biomedicine or electronics. We discuss here new important advances concerning the elucidation of the mechanism of nanoparticle formation, and the synthesis of nanoparticles with new structures or from new polymers.

Keywords Colloids · Emulsion–solvent evaporation · Miniemulsion · Nanocapsules · Nanoparticles

Contents

Abbreviations

DC-FCCS	Dual-color fluorescence cross-correlation spectroscopy
DLS	Dynamic light scattering
DMF	Dimethyl formamide

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DMSO	Dimethyl sulfoxide
FRET	Fluorescence resonance energy transfer
HFIP	Hexafluoroisopropanol
NMR	Nuclear magnetic resonance
OCTMS	Octamethylcylotetrasiloxane
PDMS-DE	Polydimethylsiloxane diepoxy terminated
PLLA	Poly(L-lactic acid)
PMMA	Poly(methyl methacrylate)
PPO	Poly(2,6-dimethyl-1,4-phenylene oxide)
PS	Polystyrene
PVAc	Poly(vinyl acetate)
PVCi	Poly(vinyl cinnamate)
PVF	Poly(vinyl formal)
SDS	Sodium dodecyl sulfate

1 Introduction

Imagine that you have synthesized a highly functional and advanced polymer. You want to formulize it as nanoparticles or nanocapsules dispersed in an organic or an aqueous medium. Unfortunately, your synthesis does not allow the use of emulsion [1, 2], miniemulsion [3], or microemulsion polymerization [4, 5] because of demanding reaction conditions. Or, let us imagine that you can perform the aforementioned polymerization in dispersed media but you cannot get rid of some residual monomer and/or initiator/catalyst without destabilizing the nanoparticles. What are the possibilities for preparation of polymer nanoparticles from your polymer?

Burton and O’Farrel addressed these issues for a variety of elastomers and resin latexes by inventing the solvent evaporation process from emulsion droplets, also called the emulsion–solvent evaporation process [6]. In this process, a pre-synthesized polymer or a mixture of different polymers are dissolved in a suitable solvent and mixed with another immiscible liquid containing a surfactant (Fig. 1). Afterwards, the solvent can be evaporated by heating the emulsion or by applying a low vacuum [7]. Two years later, Vanderhoff et al. proposed many possible examples in their patent application [8]. Thereafter, the process was adopted mainly in pharmaceutical science to encapsulate drugs in biodegradable polymers [9, 10], especially in micron-sized capsules and particles [11].

Although most of the reports deal with the preparation of microparticles, nanosized particles and capsules are also accessible, usually by employing ultrasonication to form very small droplets [12] from which the solvent is evaporated. Usually, the continuous phase is an aqueous solution. Inverse systems in which water is the solvent have been reported [13, 14] as well as non-aqueous emulsions [15] such as dimethylformamide-in-paraffin [16], dichoromethane-in-fluorinated solvent for microparticles [17], and formic acid-in-paraffin for

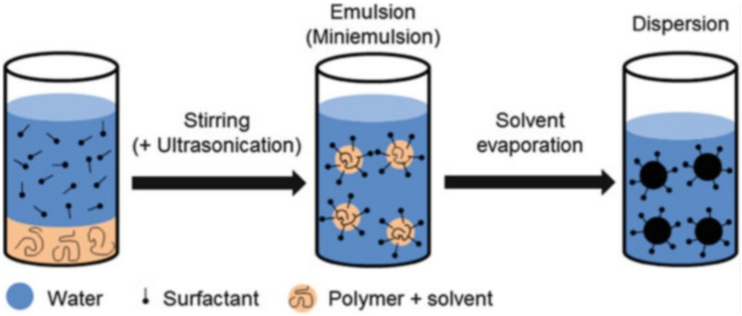

Fig. 1 In the solvent evaporation process from emulsion droplets, the polymer solvent is evaporated from droplets containing the pre-synthesized polymer. The case of a direct emulsion is depicted here, i.e., the continuous phase consists of an aqueous solution

nanocapsules [18]. Nowadays, the process is widely used to generate both micro- and nanosized particles and capsules from a wide variety of different polymers, including but not limited to semiconducting [19], biodegradable [20–22], stimuli-responsive [23] or naturally occurring polymers such as cellulose derivatives [24]. These materials are also used to encapsulate other materials such as magnetic nanoparticles [25, 26], biomaterials [27], perfluorocarbons as contrast agents for ultrasonic imaging [28, 29], dyes for up-conversion [30], or self-healing agents [31, 32] (Fig. 2). It was shown that nanocapsules with hydrophobic liquid core could be successfully fabricated with polymers having completely different thermal and mechanical properties such as poly(L-lactide), poly(methyl methacrylate), poly (phenylene oxide), poly(vinyl formal), poly(vinyl cinnamate), and poly(vinyl acetate) (Fig. 2) [31]. The use of different polymer mixtures or architectures such as polymer blends [19, 33–35], statistical copolymers [32], and block copolymers [23, 36–40] is possible. The latter polymer architecture is especially interesting for introducing an additional spatial segregation in nanoparticles to yield new multicompartment structures, such as nanocapsules or polymer particles with two or more phases, which are discussed in more detail below.

The main advantages of the process as opposed to heterophase polymerizations are its versatility with respect to the polymer that can be used, the simplicity of the method, the fast handling for the preparation of the nanoparticles, and the fact that the produced polymer dispersions do not contain any non-reacted monomers or residual initiator when the pre-synthesized polymer is purified before. The drawbacks lie in the usually broad (20–50%) size distribution of the produced particles and capsules, the usually low solid content of the dispersions, and the presence of residual surfactants. However, the last two issues can be overcome by concentrating the dispersions in vacuo [8] and by dialysis [41], respectively. Both issues were recently simultaneously solved by employing a copolymer with masked amphiphilic and pH-responsive properties. Indeed, the masked groups yielded ionic groups for electrostatic repulsion of the colloids upon reaction with water during the emulsification. The produced carboxylic acid groups were in a sufficient amount

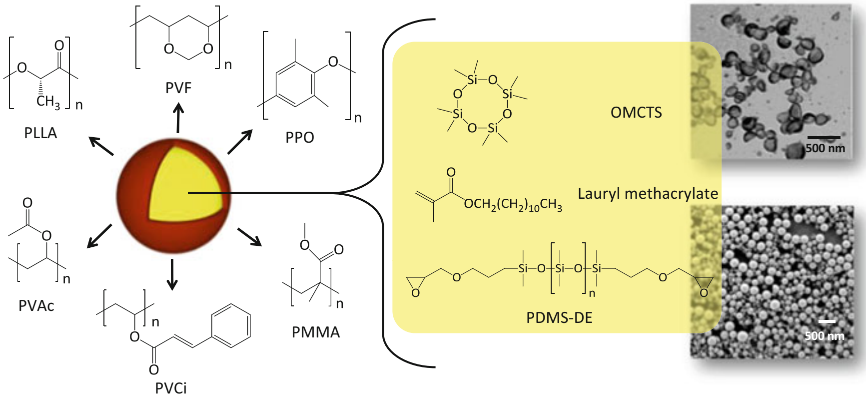

Fig. 2 Scheme showing the versatility of the emulsion–solvent evaporation technique for the preparation of nanocapsules. Polymers with completely different properties could be used to build the shell (*left*) while monomers for self-healing reactions based on various types of polymerization could be encapsulated as liquid core (*right*). *PLLA* poly(L-lactide), *PVF* poly(vinyl formal), *PPO* poly(phenylene oxide), *PMMA* poly(methyl methacrylate), *PVCi* poly(vinyl cinnamate), *PVAc* poly(vinyl acetate), *OMCTS* octamethylcyclotetrasiloxane, *PDMS-DE* polydimethylsiloxane diepoxy terminated [31]

not only to allow a reversible aggregation/re-dispersion upon changes, but also to create emulsions without additional surfactant. The solid content was increased by successive cycle aggregation/re-dispersion in a lower amount of water to concentrate the dispersion of nanocapsules. In miniemulsion polymerization, a possibility for increasing the amount of encapsulated substance without increasing the content of dispersed phase is to dilute the substance and the monomer in a solvent – instead of diluting the substance only in the monomer – and then to evaporate the solvent [42].

2 Solvent Evaporation from Nanodroplets

2.1 *Mechanism of the Emulsion–Solvent Evaporation Process*

Surprisingly little has been known for many years about the mechanisms governing the emulsion–solvent evaporation process. The main physical processes underlying the process are quite simple: a polymer is dissolved in a good solvent, which is then emulsified in an aqueous medium containing a surfactant. The slow evaporation of the polymer solvent leads to nucleation of the polymer on the water–solvent interface [12]. The mechanism for the removal of the solvent is based on its solubility in the continuous phase, therefore both the temperature and the nature of the solvent play important roles in the rate of evaporation. The completion of the evaporation can be monitored by gas chromatography [43] or NMR spectroscopy [44] and is usually realized within a few hours [45]. The role of the evaporation on the hardening kinetics of the particles plays an important role, provided that the continuous phase is saturated with the solvent mainly present in the dispersed phase and that the diffusion rate of the solvent of the dispersed phase in the continuous phase is fast compared with the solvent evaporation kinetics. In an experimental study performed with dichloromethane, ethyl acetate, and acetonitrile as solvents, Wang and Schwendeman demonstrated that the rate-limiting step for mass transport of solvent depends on the properties of the solvent [43]. Dichloromethane at room temperature is found to be liquid-side transport limited whereas ethyl acetate and acetonitrile were gas-side transport limited. As expected, the evaporation rate was largely affected by the diameter of the impeller, its rotational speed, and the temperature. The particle's hardening profile could be determined and predicted without needing to measure the concentration of polymer in the solvent in time, but by measuring the concentration of the solvent and by knowing the permeability coefficient of the solvent at the liquid–air interface [43]. After evaporation of the solvent, the dispersions can be dialyzed to remove unwanted or low molecular weight polymer and can be freeze-dried.

One of the most critical properties of nanoparticles is size, hence its control is of outmost importance. Because the particles are formed from droplets, their size is largely dependent on the droplet size. In the case of miniemulsions, the size of the droplets is controlled by the concentration of surfactant [40]. Other parameters such as the nature of the solvent [46], the stirring rate, or ultrasonication time [47] also influence the particle size and particle size distribution. Longer and/or stronger emulsification usually leads to smaller and more narrowly distributed particle size to a certain extent [47]. However, it is difficult to ascribe an observed effect upon changing one parameter to this sole parameter, because most of the parameters are not independent.

Physical processes responsible for the destabilization of emulsions such as Ostwald ripening and coalescence are of crucial importance for the determination of the final particle size and size distribution. It is known that the addition of a small amount of a chemical that is preferentially soluble in the dispersed phase can hinder the Ostwald ripening process [48]. This chemical, sometimes called the osmotic pressure agent because it allows the building of an osmotic pressure upon possible change of chemical composition of the droplets upon Ostwald ripening, is usually a low molecular weight substance that is insoluble in the continuous phase. Thereby, it counteracts the Laplace pressure of the droplets and stabilizes the emulsion droplets. In the solvent evaporation process, no osmotic pressure agent is normally added as the polymer itself can act as osmotic pressure agent because it is insoluble in the continuous phase. However, the concentration of polymer must be above a threshold value to effectively hinder Ostwald ripening [49]. Loxley and Vincent have supposed that the relatively broad size distribution of the obtained particles is caused by coalescence [50]. Dynamic light scattering (DLS) was employed to measure the size of emulsion droplets and the obtained nanoparticles [45]. Based

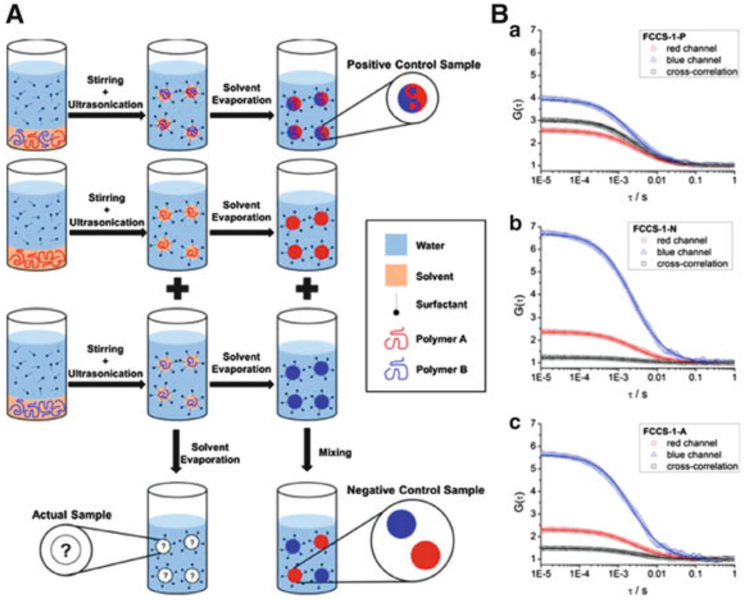

Fig. 3 (**A**) Scheme of the preparation of the samples for both DC-FCCS and FRET investigations. The *colors* represent two different polymers or two differently labeled polymers. (**B**) Correlation curves (*scattered symbols*) and corresponding fits (*lines*) of the DC-FCCS samples: FCCS-1-P positive control sample (*a*), FCCS-1-N negative control sample (*b*), and FCCS-1-A actual sample (*c*) [52]

on these measurements, it was concluded that coalescence plays an important role in particle formation under certain conditions. However, it was shown recently by dual-color fluorescence cross-correlation spectroscopy (DC-FCCS) that coalescence is not significant if the droplets are sufficiently stabilized [51, 52]. Emulsion droplets were separately labeled with two different dyes and mixed (Fig. 3a). The solvent was evaporated to yield nanoparticles and the cross-correlation curves of the temporal evolution of the fluorescence intensity of the labeled nanoparticles were determined by DC-FCCS (Fig. 3b). The amount of double-labeled nanoparticles was measured to be below 10% and therefore significant coalescence did not occur and could not be found responsible for the large size distribution of particles fabricated by the emulsion–solvent evaporation technique as calculated by simulations [52]. Thus, the rather broad particle size distribution probably originates from the emulsification step, pointing out that further development of the process is needed to yield monodisperse nanoparticles. DLS measurements were not conclusive and yield only indirect insight on coalescence. On the contrary, fluorescence resonance energy transfer (FRET) and DC-FCCS measurements allow the direct determination of extent of coalescence either qualitatively or quantitatively, respectively [52].

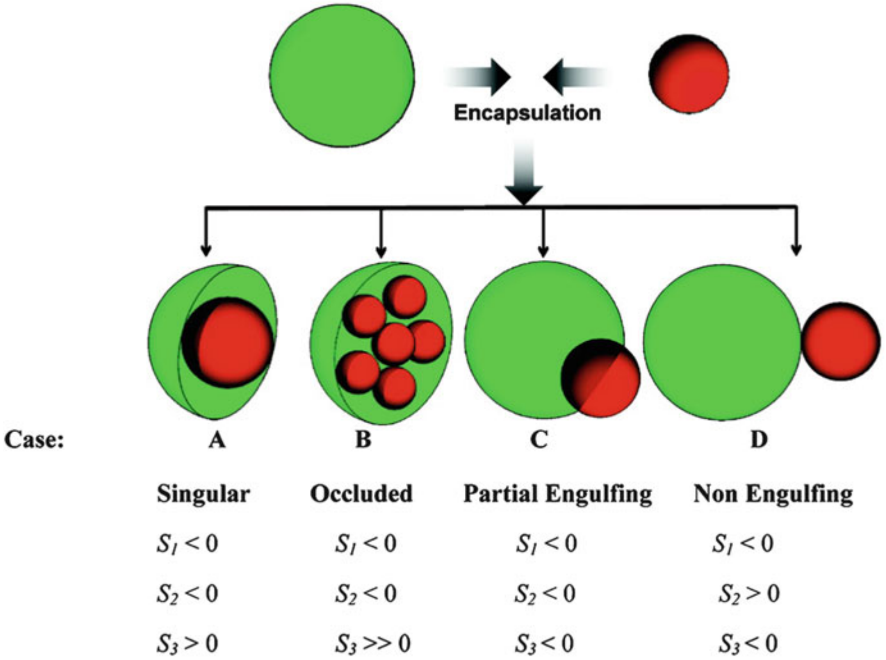

Fig. 4 Morphologies obtained for three immiscible liquids in colloidal systems for cases *A*–*D* with different combinations of positive and negative spreading coefficients (S_1, S_2, and S_3). Reprinted with permission from [55]. Copyright 2011 American Chemical Society

2.2 Colloidal Structures

Torza and Mason formulated a general theory describing the thermodynamically stable morphologies obtained when three immiscible liquids are mixed, with two of them present in a dispersed phase, using the spreading coefficient S_i that depends on the interfacial tensions of the oil and water phases according to $S_i = \gamma_{jk} - (\gamma_{ij} + \gamma_{ik})$ [53]. This theoretical value can be employed to predict morphologies of micro- or nanoparticles consisting of two immiscible materials. Depending on the sign of the spreading coefficients, one of the substances can be completely (Fig. 4a), partially (Fig. 4c), or not at all (Fig. 4d) engulfed in another material. Occluded structures (i.e., with multicores) are also possible morphologies and can be obtained as a kinetically trapped structure or as a thermodynamically favorable structure when crosslinking is applied in the dispersed phase [54].

In general, the final morphology will be the one with the lowest free Gibbs enthalpy (G_s), which can be calculated by:

$$G_s = \sum_{i,j}^{n} \gamma_{ij} A_{ij} \tag{1}$$

in which γ_{ij} represents the surface tension of the phases i and j, and A_{ij} represents the area of the interface. Therefore, the ratio of the different phases and the amount of surfactant are of outmost importance for the determination of the final particle morphology. In the case of nanoparticles of a binary blend of a hole-transporting and an electron-transporting polymer, the composition of both phases (i.e., the distribution of one polymer in the other one in the two phases) followed the prediction of the Flory–Huggins theory [56]. The quantum efficiency of devices produced with the nanoparticle blend were found to be improved compared to other methods [57].

However, what happens if G_s cannot be minimized and is stuck in a local minimum on the energy landscape? In this case, the morphology is kinetically but not thermodynamically stable. In addition, other factors such as the crystallization of polymers can also significantly influence the particle morphology [41, 58]. Chen et al. showed that the viscosity of the liquids played a significant role in the morphology of particles composed of polystyrene (PS) and poly(methyl methacrylate) (PMMA) [59]. Indeed, PMMA partially encapsulated PS for high molecular weight polymers whereas the contrary was observed for low molecular weight polymers. Okubo et al. investigated the effect of different stabilizers on the morphology of PS/PMMA particles [33]. Particles stabilized with poly(vinyl alcohol) displayed small dimples whereas for SDS acorn and spherical structures with increasing amount of SDS were observed. Both phenomena were explained by the interplay of solvent evaporation and stabilization by the surfactant. Although high amounts of SDS stabilized both the PS and the PMMA interfaces to water equally well, this was not the case for smaller amounts. Therefore, bowl-like PMMA shells were formed, in which the PS slowly hardened upon further evaporation of the solvent. As the PS contracted because of the ongoing evaporation of solvent, bowl- or dimple-like structures were obtained. These effects were not observed when dichloromethane was used instead of toluene as solvent to be evaporated. This was explained by the fact that toluene is preferentially partitioned in the PS phase, which is not the case for dichloromethane. The molecular weights of the PS and PMMA were also found to play a role on the morphology [34]. Whereas the interfacial tension polymeric droplet against aqueous phase was not dependent on the molecular weight, the interfacial tensions between PS and PMMA in the droplets increased with increasing molecular weight and snowman-like particles could be obtained for high molecular weight polymers.

Besides the well-known core–shell and inverse core–shell [60], or acorn and Janus morphologies obtained with polymers with similar polarities [33], other interesting structures can be formed. Half-spherical structures are accessible by removing the liquid in acorn structures formed with a polymer and a liquid [40, 61]. Onion-like structures are created from block copolymers, for which the phase separation into lamellae causes layered structures that follows the curvature of the particle where they are confined [37, 40, 62]. The diameter of the particle is in this case also very important. Indeed, if the particle size is low enough, core–shell or Janus structures can be obtained [40]. A large variety of different structures were predicted from simulations on diblock copolymer/homopolymer blends [63], star-triblock copolymers in spherical nanopores [64], or on diblock copolymers under different confinements [65–67], among which several have already been prepared

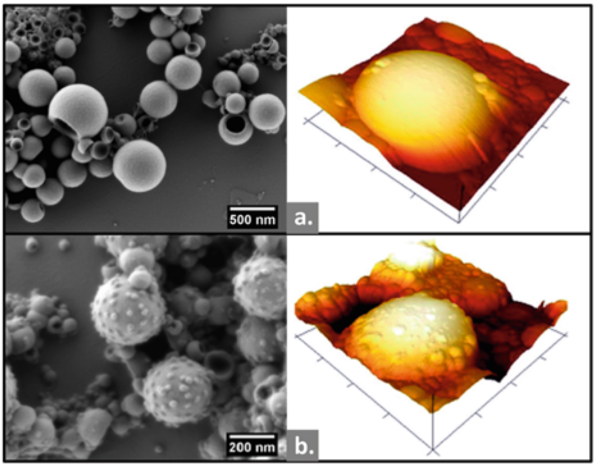

Fig. 5 SEM micrographs (*left*) and 3D perspectives of SFM height images (*right*) of (**a**) patchy nanocapsules of poly(methyl methacrylate-*b*-vinyl ferrocene) and (**b**) the nanocapsules after oxidation with $KMnO_4$. Reprinted with permission from [23]. Copyright 2012 American Chemical Society. The surface of the nanocapsules is relatively smooth before oxidation and presents outgrowths after the selective oxidation of the poly(vinyl ferrocene) patches with $KMnO_4$

by the emulsion–solvent evaporation process. However, these theoretical studies clearly show that many more interesting and highly complex morphologies could be still prepared.

Kinetic morphologies are formed once the free Gibbs energy G_s cannot be minimized to its global minimum, but only to a kinetically stable local minimum. The main reason for a kinetically trapped morphology is a hindered phase separation of the materials inside the particle. This phenomenon can occur when high molecular weight polymers are employed in the process. As diffusion of the chains is necessary for phase separation, one possibility to obtain kinetically trapped morphologies is to increase the viscosity of the polymeric emulsion droplets [68]. One possibility to control the viscosity inside the droplets of polymeric emulsions is to vary the molecular weight of the polymer or the solubility of the polymer in the chosen solvent. Additionally, both the evaporation temperature and the evaporation rate of the solvent are of high importance for the build-up of a thermodynamically stable morphology [36, 37, 69]. However, structures that resemble kinetically trapped morphologies can also be thermodynamically stable when specific ratios of block length in the block copolymers are achieved [23] or if the phase separation occurs in the weak segregation limit [40]. Both cases were used for the generation of patchy nanoparticles and nanocapsules. Functional patchy nanocapsules of poly(methyl methacrylate-*b*-vinyl ferrocene) could be selectively reacted with oxidants to yield different structures (Fig. 5). The concept of multicompartmentation – with many polyvinylferrocene compartments in the form of patches in the nanocapsules shell and one compartment created by the

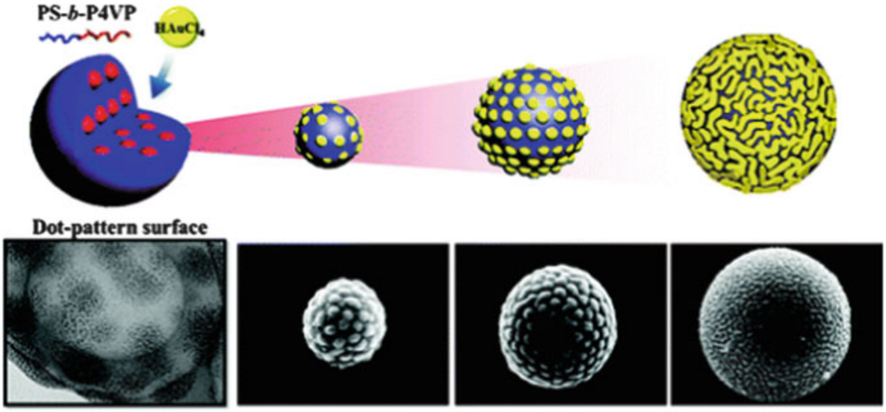

Fig. 6 Scheme (*top*) and SEM micrographs (*below*) showing the morphologies of particles composed of gold nanoparticles (*$HAuCl_4$*) and poly(styrene-*b*-4-vinylpyridine) (*PS-b-P4VP*) with different diameters. The structures evolved from discontinuous gold domains to quasi-continuous domains when the particle size increased from ~250 to 1,200 nm. Reprinted with permission from [81]. Copyright 2012 American Chemical Society

liquid core and forming a reservoir for the subsequent release of chemicals – was married with the concept of stimuli-responsive materials. Indeed, chemicals could be released from the reservoir compartment by selective oxidation of the responsive patches of poly(vinyl ferrocene) [23].

As previously mentioned, multicompartment morphologies [69] were easily be obtained by using block copolymers [23, 36–40, 62, 71–76]. Such structures can be further compartmentalized by adding inorganic nanoparticles that preferentially migrate to one domain [77, 78].

The obtained structures can be isotropic, i.e. the metal nanoparticles segregate in one type of lamellae in onion-like nanoparticles [78–80], form isotropic surface structures [81, 82] (Fig. 6), or can be anisotropic with regard to the particle geometry. The latter case was based on metal nanoparticles/polymer assemblies [81] or similar assemblies but with a fluorescent dye instead of the metal nanoparticles [83].

Isojima et al. also showed that by varying the ratio of metal nanoparticles to polymer matrix one can obtain both isotropic and anisotropic morphologies [84]. Another way of adding further or changing existing compartments is the removal of one compartment, for example by a selective solvent [85, 86].

In addition, the solvent evaporation from emulsion droplets can also be used on non-polymeric materials [87, 88] such as inorganic nanocrystals of $BaCrO_4$ and others dispersed in an organic solvent. Upon emulsification and evaporation of the organic phase, spherical aggregates of the nanocrystals are formed. This method has also recently been exploited to prepare manganese ferrite/graphene oxide nanocomposites [89] and siRNA-loaded magnetic metal nanoparticles [90].

Among different possible morphologies, capsules (i.e., core–shell particles with one liquid core) are often targeted morphologies for the protection and encapsulation of substances. When nanocapsules are produced from the emulsion–solvent evaporation process, the liquid core material is usually non-functional. However, functional non-solvents can also be used, for example in the form of self-healing agents [31, 32] or of pH-responsive non-solvent [91]. The encapsulation of Grubbs catalysts of monomers for a self-healing reaction based on ring-opening metathesis polymerization by the mild emulsion–solvent evaporation method was found to be advantageous over other methods. Although silica nanocapsules with a hydrophobic liquid core are porous and therefore cannot be used as fillers in a hydrophobic matrix [92], it was not possible to encapsulate Grubbs catalysts in nanocapsules fabricated by free-radical polymerization in miniemulsion polymerization [91]. Furthermore, whereas in interfacial step-growth polymerization the functional units in the monomers needed to form the polymer shell can react with sensitive products such as catalysts [94], the polymer building the nanocapsules shell can be relatively chemically inert. For the pH-responsive core, tertiary amines with long alkyl chains were embedded as liquid core in nanocapsules and could be released to the continuous phase after protonation of the amine [91]. The diffusion of the core out of the nanocapsules allowed for an unprecedented chemical transformation of the liquid core from hydrophobic to aqueous. Finally, swollen PMMA nanocapsules prepared by the emulsion–solvent evaporation technique could be elongated to a core–shell ellipsoidal shape in an electrospinning jet [95].

2.3 Effect of the Nanoconfinement

Because the polymer nanoparticles prepared by the emulsion–solvent evaporation process are highly pure, they are ideal samples for investigating the effect of nanoconfinement on polymer properties such as crystallization. For the crystallization of poly(ethylene oxide) nanoparticles after evaporation of water from inverse miniemulsions, a large supercooling was detected compared to the bulk material [13]. Upon removal of water from the dispersion, the loosely packed poly(ethylene oxide) lamellae slid apart, possibly generating single crystals. Recently, the crystallization of semicrystalline polymers such as syndiotactic and isotactic polystyrene as well as poly(L-lactic acid) (PLLA) was investigated [41]. For all polymers, a decrease in crystallinity with decreasing particle diameter was observed. Both syndiotatic and isotactic polystyrene nanoparticles showed anisotropic structures because the crystallization induced a deformation of the otherwise spherical particles (Fig. 7a, b). For PLLA, it was even possible to control the crystallinity by heating the aqueous dispersion because PLLA cold-crystallizes below 100°C. The extent of cold-crystallization upon heating the PLLA particles was found to be larger for smaller particles than for the larger ones (Fig. 7c).

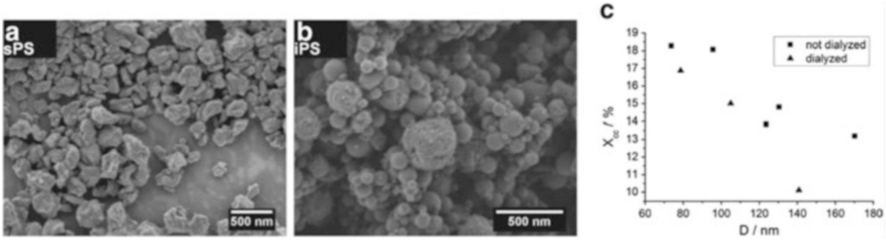

Fig. 7 SEM micrographs of (**a**) syndiotactic polystyrene and (**b**) isotactic polystyrene showing non-spherical strcutures due to the crystallization of the polymers in the dispersed state during the emulsion–solvent evaporation procedure. (**c**) Evolution of the cold-crystallization of PLLA in particles prepared by the emulsion–solvent evaporation process in dependence on the particle diameter [41]

2.4 *New Emulsions*

Whereas the preparation of particles with solvent evaporation from apolar droplets is widely reported, their preparation from polar droplets is still unusual [13–18]. The challenge is to find a suitable polar solvent with a low boiling point that can solubilizes both the polymer and the substance to be encapsulated. Water as dispersed phase in such cases is not always suitable and has been replaced in non-aqueous emulsions by other polar solvents [15] to allow reactions sensitive to water such as anionic polymerization [96] or reactions requiring high temperature and the absence or removal of water [97]. Dimethyl formamide (DMF), formic acid, formamide, or dimethyl sulfoxide (DMSO) are polar solvents that can be used but that are difficult to remove because of their high boiling points. Recently, hexafluoroisopropanol (HFIP) was proposed as a suitable candidate for the preparation of polymer nanoparticles via the emulsion–solvent evaporation method. It also has the ability to be a good solvent for metallopharmaceuticals that need to be embedded in a carrier material to be delivered in the body [98]. A ruthenium nitrosyl complex designed for phototherapy that is polar but not soluble in water could be successfully encaspulated in polymer nanoparticles after the evaporation of HFIP from HFIP-in-alkane miniemulsions (Fig. 8) [99]. Various polymer matrixes such as gelatin, PLLA, poly(ethylene terephtalate), and poly(vinyl formal) could be used for the physical entrapment of complex. The colloidal stability of the particles was improved by matching the density of the continuous phase to the density of HFIP, and hence *cis*-decalin was found to be more suitable than cyclohexane, hexadecane, and isooctane. The nanoparticles could be re-dispersed in aqeuous solutions after removal of the alkane, and the release of nitric oxide upon irradiation of the aqueous dispersion with a low intensity UV light could be demonstrated in a fluorescence assay.

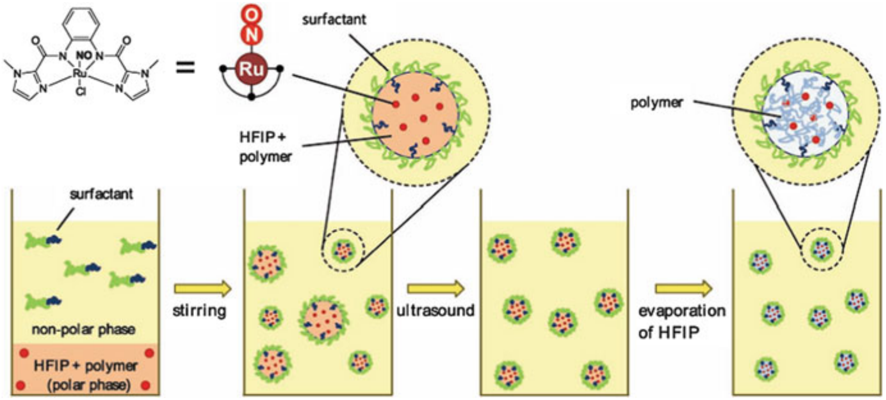

Fig. 8 Encapsulation of a ruthenium nitrosyl complex in polymer nanoparticles in non-aqueous hexafluorisopropanol (*HFIP*)-in-alkane miniemulsion [99]

3 Summary, Conclusions, and Outlook

The main challenges in colloid chemistry nowadays are oriented towards the strategic fields of health and medicine, energy and resource savings, and the design of so-called smart materials allowing the automation of tasks without human intervention. The colloids recently prepared have gained increased complexity either in their shape, chemistry, and/or functions and their design has been largely inspired by the cellular and subcellular systems present in nature. This is the case for the block-copolymer assemblies in nanoparticles and nanocapsules that allows for the coexistence of multicompartmentation and stimuli-responsive exchange of chemicals in the same objects. Because the increase in complexity can be achieved by colloid engineering but also by the subsequent utilization of other processes such as electrospinning of nanoparticles [100], the portfolio of achievable structures is almost unlimited.

A very interesting combination for the preparation of complex nanoparticles is the use of miniemulsions droplets as templates to perform the evaporation of the solvent. Indeed, miniemulsions are particularly stable colloidal systems without significant mass transfer between the droplets, which in turn can be precisely tuned by the concentration of the surfactant. It has been shown that the solvent evaporation process from miniemulsion droplets is uniquely suited to prepare a wide variety of single- and multicompartment nanoparticles and nanoparticles with unprecedented properties. Furthermore, it was shown that the coalescence between miniemulsion droplets does not significantly affect the size distribution of the final nanoparticles obtained by the miniemulsion–solvent evaporation method [52]. Recently, the process of emulsion–solvent evaporation has been significantly improved by the emulsification step being possible without surfactant, and the solid content being increased by successive and reversible aggregation/re-dispersion steps.

Because the emulsion–solvent evaporation is versatile, new nanoparticles structures and nanoparticles from new materials are expected to be reported. Open questions such as how to create very monodisperse nanoparticles via this technique and the influence of the molecular state of the polymer on the nanoparticle and nanocapsule properties such as permeability are expected to be answered in the foreseeable future, helping to create more functional and useful materials.

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