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One step generation of single-core double emulsions from polymer-osmose-induced aqueous phase separation in polar oil droplets†

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Water-in-oil-in-water emulsions (W/O/W) are aqueous droplet(s) embedded within oil droplets dispersed in a continuous water phase. They are attracting interest due to their possible applications from cosmetic to food science since both hydrosoluble and liposoluble cargos can be encapsulated within. They are generally prepared using a one-step or a two-step method, phase inversion and also *via* spontaneous emulsification. Here, we describe a general and simple one-step method based on hydrophilic polymers dispersed in polar oils to generate osmose-induced diffusion of water into oil droplets, forming polymer-rich aqueous droplets inside the oil droplets. Polyethylene glycol, but also other hydrophilic polymers (branched polyethylene imine or polyvinyl pyrrolidone) were successfully dispersed in 1-octanol or other polar oils (oleic acid or tributyrin) to produce an O/W emulsion that spontaneously transformed into a W1/O/W2 emulsion, with the inner aqueous droplet (W1) only containing the hydrophilic polymer initially dispersed in oil. By combining single drop experiments, with macroscopic viscosity measurements, we demonstrated that the double emulsion resulted of water diffusion, which amplitude could be adjusted by the polymer concentration. The production of high internal phase emulsions was also achieved, together with a pH-induced transition from multiple to single core double emulsion. We expect this new method for producing double emulsions to find applications in domains of microencapsulation and materials chemistry.

1 Introduction

Double emulsions (W/O/W) are attractive for technological applications owing to their ability to gather apolar and polar phases in a single compartment, then affording encapsulation of both hydrophilic and hydrophobic cargos.[1] They were initially produced *via* a two-step method[2] that consists of preparing water-in-oil (W/O) emulsions that are further emulsified in water. This requires the use of hydrophilic and lipophilic emulsifiers that span at both interfaces. A relatively high amount of the lipophilic emulsifier is then needed to prevent release of the internal aqueous droplet during the second emulsification step.[3–14] This method allows a facile encapsulation of hydrophilic cargos, dispersed in the initial

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W/O droplets. An alternative method was developed recently affording a one-step preparation of such emulsions by using blends of surfactants or amphiphilic polymers.[3,15–26] This method is more attractive than the two-step route, owing to its simplicity. However, because they are obtained by simply mixing oil and water (and emulsifiers), the aqueous inner droplet of the double emulsion has the same composition as the one of the continuous phase. Therefore, the encapsulation of cargos is much less efficient, mostly remaining in the outer phase. Another approach is the spontaneous emulsification that still proceeds in one-step and is achieved by osmose-induced diffusion of water in oil droplets. This was first observed when forming oil droplets in water stabilized by amphiphilic polymers that also contained salts, dispersed in oil, which contributed to the formation of small aqueous droplets within oil.[7,20–30] Another way to produce double emulsion is to use microfluidics,[31] yet affording encapsulation of hydrophilic cargos by dispersing them in the initially produced water droplets in oil. Although this method still yields low amounts of final materials, it revealed of interest for producing polymersomes, liposomes, or polyelectrolyte capsules upon dewetting.[32–47] Interestingly, oil-free double emulsions can also

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be produced from water-in-water emulsions, either by micro-fluidics, or by osmose-induced reverse diffusion of water in polymer-rich droplets.[48,49] For instance, a droplet made of a mix of miscible pair of polyethylene glycol (PEG) and Dextran (both at relatively low concentration) dispersed in a continuous phase containing PEG at higher concentration induces diffusion of water from the inner droplet to the more concentrated PEG outer continuous phase. The concentration of both polymers PEG and Dextran increases in the droplet, which further phase separate, forming a 'water (PEG)'-in-'water (Dextran)'-in-'water (PEG)' double aqueous emulsion. Higher order aqueous emulsions can also be produced by this approach based on water diffusion.[50]

Based on this, we hypothesized that dispersing hydrophilic polymers in oil and pouring this mixture in water could induce formation of an aqueous droplet within the oil droplet upon water diffusion to equilibrate osmotic pressure. Here, we show that this mechanism actually occurred for several oils (octanol, tributyrin or oleic acid) containing different hydrophilic polymers (PEG, branched polyethylene imine or polyvinyl pyrrolidone), which were successfully solubilized within. Dispersing these oily solutions in aqueous solutions, in which polyvinyl alcohol (PVA) is added to help stabilizing the oil droplets,[51] spontaneously yields to W1/O/W2 single core double emulsions: as shown below, the W1 phase is then enriched in the hydrophilic polymer initially dispersed in oil, while the W2 phase contains the PVA polymers. We also report experiments at the scale of a single oil drop evidencing the diffusion of water, and show how the stability and rheology of the final double emulsions depend on the phase fractions and polymers concentrations. Additionally, We extended our approach to PNIPAM-COOH co-dispersed in oil with PEG in order to stabilize multiple core double emulsions when deprotonated (in basic PVA solution), which turned into single core double emulsions when the pH was decreased.

2 Material and methods

All chemicals were from Sigma-Aldrich. Polyethylene glycol/PEG (20 kDa) was dispersed in 1-octanol by heating and shaking samples at 80 to fully solubilize the polymer. As well, branched polyethylene imine/bPEI (30 kDa) and polyvinyl pyrrolidone/PVPone (40 kDa) were also dispersed overnight in 1-octanol, but without heating. For PEG and PVPone, the tested concentrations are typically between 0 to 20 wt%. Polyvinyl alcohol/PVA (Mowiol 4–88, 31 kDa) was weighted and water was added to get a 10 wt% concentration, this solution was further heated at 70 for one hour, and shaken overnight.

Emulsions samples were observed either by dark field or epifluorescence microscopies. In the first case, an Eclipse microscope (Nikon) working in reflection and equipped with a dark field condenser was used. The Nikon oil immersion microscope objective was 40× with a numerical aperture (N. A.) of 0.80. Images were acquired with an Iris 9™ Scientific CMOS camera (2960 × 2960 pixels) and further treated with Image-J.

Epifluorescence imaging was performed on a Leica DMI 4000B inverted microscope equipped with a ×40 lens (HCX PL APO, 1.4 NA) and a CoolLED light source combined with appropriate filter cubes to select the excited and emitted fluorescence wavelength range. Images were acquired using MicroManager and processed with Image-J.

For the single drop technique, we performed the experiments with the Tracker instrument from Teclis Scientific. In practice, due to differences in density, we used the rising-drop configuration; this is obtained by using a curved syringe, allowing to create a oil drop rising within a water phase. The typical size of the drop is 1 mm and the typical volume is of the order of 10 μL. The surface tension is then obtained by fitting the shape of the curve by the Young-Laplace equation.

We used a MCR301 apparatus from Anton Paar for the rheological studies. Experiments were performed with a plan–plan geometry with a diameter of 75 mm, while the sample is within a gap of 1 mm. Typical flow curves are performed, measuring the sample viscosity as a function of the applied shear rate.

3 Results and discussion

3.1 Emulsion preparation and characterization

Once PEG was dispersed in 1-octanol, we observed that these oily transparent liquid solutions gelled when cooling (Fig. 1).

This sol–gel transition was quantitatively investigated by rheological oscillatory measurements. Ramps of temperatures were performed at a fixed amplitude (5%) and frequency (1 Hz). In the gel phase, an elastic modulus was measured, and it vanished at high temperature. Note that different behaviors are found under cooling and heating (Fig. 2). Still, we can well identify a sol–gel transition, under cooling, at around $T = 40\ ^\circ$C. With PEG, the emulsification procedure was then performed at 70 $^\circ$C, above the temperature transition. Emulsions were then prepared by pouring hot PEG-octanol dispersions in a PVA
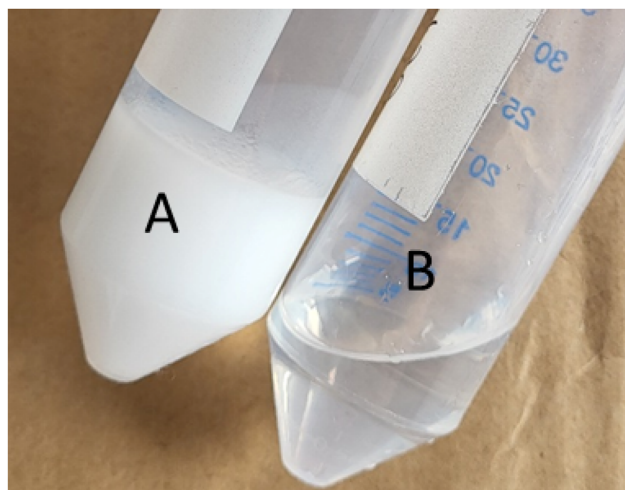

Fig. 1 Pictures of the samples of PEG dispersed in 1-octanol at room temperature (A) and 70 (B).
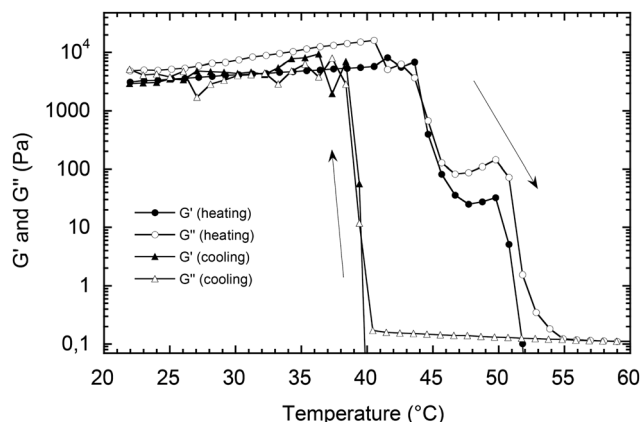
Fig. 2 Viscoelastic moduli (G' and G'') of the PEG/octanol mixture, under heating and cooling.

solution at 10 wt%. The relative volumes of both the oily octanol phase and aqueous PVA phase could be changed to produced more or less dilute emulsions. For all the emulsions, the samples were vigorously mixed by a vortex apparatus for 30 s, and observed by microscopy after a couple of minutes.

The use of Nile red initially dispersed in octanol-PEG allowed the detection of this apolar phase by epifluorescence. We first observed that PEG-free octanol-in-PVA stable emulsions were formed with pure octanol droplets embedded in the aqueous continuous PVA-rich phase (Fig. 3A). Upon increasing the amount of PEG initially dispersed in 1-octanol, droplets appeared within the oily droplets. These internal droplets lacked fluorescence confirming that aqueous droplets were formed within oil (Fig. 3B and C). At low amount of PEG (2.5 wt%), a few droplets were observed within oil droplets (Fig. 3B), forming multiple-core emulsions. At 5 wt% PEG, the number and diameter of aqueous droplets within oil droplets increased, forming both multiple- and single-core double

emulsion droplets (Fig. 3C). An ideal single-core double emulsion was obtained for 10 wt% PEG initially dispersed in 1-octanol with mainly a single aqueous droplet within oily ones (Fig. 3D).

Other combinations of polymers and oils provide such a formation of single-core double emulsions when poured in PVA, as described above in the case of PEG-octanol. For instance, dispersing bPEI or PVPone (14 and 10 wt%, respectively) in pure 1-octanol was successfully achieved, with solutions remaining liquid at room temperature, and double emulsions could then be produced without heating. As well, oleic acid and tributyrin in which PEG was dispersed also formed double emulsions. As for 1-octanol, these solutions were limpid at 70 °C, but gelled upon cooling. By contrast, when PEG was dispersed in dichloromethane, not any kind of double emulsion was obtained when poured in PVA, probably because that solvent is too hydrophobic and does not allow diffusion of water within. We expect that in this case, PEG is released in the PVA outer continuous phase.

In order to fully characterize the repartition of the components in the double emulsions, we synthesized fluorescent PEG from diamino-PEG derivative using FITC (fluorescein isothiocyanate) and mixed this dye with octanol-PEG to be further poured in hot PVA. The resultant double emulsion showed droplets having a highly fluorescent core, surrounded by a non-fluorescent shell, all in a very slightly fluorescent background (Fig. 4A). In parallel, when sulforhodamine B was initially dispersed in PVA, the resulting double emulsion (prepared without using PEG-FITC) showed droplets lacking fluorescence, all embedded in a continuous highly fluorescent background (Fig. 4B), meaning that the chemicals initially dispersed in the continuous water phase are not recovered in the droplets. Altogether, the images on Fig. 4A and B show that the internal droplets, within the oil droplets, are indeed made of an aqueous phase with PEG dispersed within and not containing PVA. As well, PEG no longer remained within the 1-octanol since the outer shell around the internal droplet clearly lacked fluorescence. Note though that small amount of PEG was released in the outer PVA continuous phase, accounting for the slight outer fluorescence. This observation also confirms that water diffuses through octanol, affording hydration of the PEG within, and formation of aqueous droplets in oil, and then, a double emulsion.
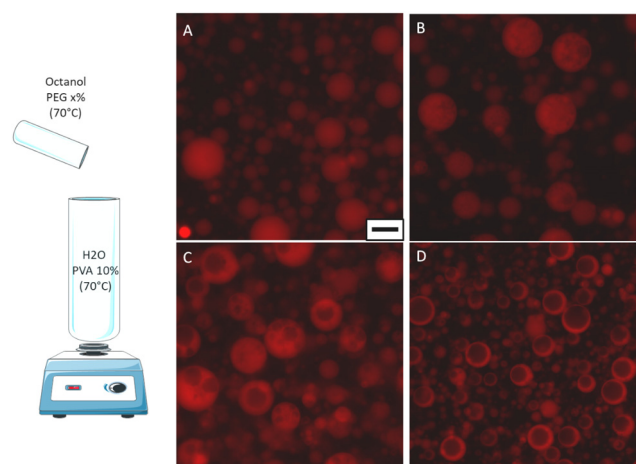

Fig. 3 Schematic representation of the experiment to produce double emulsions (left). Right: Epifluorescence images (A)–(D) for emulsions produced with x = 0, 2.5, 5 and 10 wt% PEG in 1-octanol, respectively. The scale bar is the same for all images and stands for 20 μm. The initial oil fraction is 0.25.
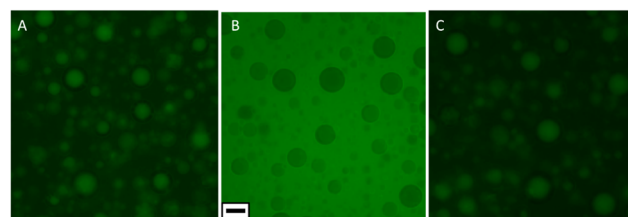

Fig. 4 Epifluorescence images for emulsions prepared as described in the main text with (A) PEG-FITC dispersed in 1-octanol; and sulforhodamine B dispersed initially dispersed in (B) PVA and (C) 1-octanol. The scale bar is the same for all images and stands for 20 μm.

For more information, we planned to disperse hydrosoluble dyes, like sulforhodamine B or BSA (bovin serum albumin)-FITC into the oily phase. It required adding water and butanol in the PEG-octanol phase: with these additives, a microemulsion can successfully be obtained in the oil phase. An optimal composition of this oily phase was then PEG (10%) in octanol (25 mL)–butanol (5 mL) plus water (200 μL). Interestingly, the dispersion was limpid and fluid at room temperature, no longer gelling upon cooling as in the case of water and butanol free mixtures.

In this oily phase, thanks to the microemulsion, we then could first disperse sulforhodamine B or BSA-FITC, showing that hydrosoluble components, together with PEG, can be entrapped in the octanol phase. Then, after the formation of the double emulsion by pouring such dispersion in an aqueous phase containing PVA, fluorescence was mainly observed in the internal droplet, demonstrating that these dyes ended with PEG within the internal aqueous droplet (Fig. 4C). All these results with dyes confirm that the composition of the internal aqueous droplet was different from that of the external aqueous continuous phase, and show that water does not enter within oil droplets upon simple mixing as it is generally the case when preparing double emulsion via a single step method. Rather, water – and only water – diffuses through the oil, hydrating polymers that further form aqueous polymer-rich droplets within oil, eventually entrapping all other hydrosoluble chemicals initially present in the oily phase. Obviously, our method then allows bulk - with no limits on volumes – one-step preparation of W1/O/W2 double emulsions, with the inner aqueous medium, W1, of different composition than that of the external continuous phase, W2.

3.2 Drop scale experiments

To gain complementary information on the formation of the internal water droplet in oil, we performed experiments at the scale of single drops. First, we used the rising drop method, in which a millimeter drop of 1-octanol is hold at the tip of a syringe, surrounded by water with PVA. Without added polymers in 1-octanol, the drop was always transparent. The setup also allowed us to measure the surface tension by analyzing the shape of the drop: we obtained a surface tension of 3 mN m^{-1}, a value smaller than that of the pure octanol/water (7 mN m^{-1}) meaning that PVA significantly adsorb at the interface. When PEG or PVPone was added in 1-octanol, the drop became dark within a few minutes (Fig. 5). Tiny objects were created at the

interface, fell down into the oil drop due to gravity and accumulated at the bottom of the drop. Finally, the drop ended dark in transmission, due to the scattering by the created objects. The oil drop could eventually be detached from the syringe and carefully observed under the microscope, revealing that the tiny objects appearing in the oil drop were water droplets.

Note that the surface tension was also measured during this water diffusion process, and did not change; therefore, only PVA molecules adsorb from the outer water phase, and nothing is adsorbed from the inside of the drop. To better visualize the polymer-induced transfer, we studied what happened when a drop of 1-octanol was put into contact with the top of a solution of water and PVA. Here again, when no polymers were added to 1-octanol, the drop simply floated and remained transparent at the surface. When PVPone was added in 1-octanol, we observed that water droplets instantaneously get incorporated inside the oil drop. Moreover, in this experiment which includes an interface with air, evaporation of 1-octanol occurred and induced Marangoni flows within the oil drop.[52] As a consequence, the smallest incorporated water droplets get trapped in the toroidal flows and follow the Marangoni-driven recirculation. In parallel, a large water droplet stays in the center of the oil droplet. The Movie S1 in ESI† shows both the presence of water droplets in the oil one, and their Marangoni recirculation due to 1-octanol evaporation.

3.3 Effect of the polymer concentration on droplet size and emulsion viscosity

We had observed that the size of the inner water drop depends on the concentration of PEG initially dispersed in 1-octanol (Fig. 3). In fact, water diffusion within 1-octanol ends when osmotic pressures are equilibrated between the internal PEG-rich water droplet and the outer continuous aqueous phase containing PVA (the shell of octanol thus acting as a membrane). Therefore, increasing the polymer concentration in oil induces more diffusion, and is a way to control the internal droplet size. A direct consequence of such a water transfer towards the oil is also that the volume fraction of the continuous phase (water with PVA) decreases, while the one of the dispersed phase (octanol, with its internal water droplet) increases. For any emulsion, its viscosity is strongly dependent on the volume fraction of the different phases, especially when the fraction of the dispersed phase is higher than 0.5. The widely-used Krieger–Dougherty law states that the relative viscosity (dispersion viscosity divided by the continuous phase viscosity) only depends on the volume fraction of the dispersed phase.[53] Therefore, any change in volume fraction, due to a transfer of water towards the oil droplet, should be monitored by rheological measurements. We thus performed viscosity experiments on our double emulsions, with a fixed initial oil fraction (0.5), but for various polymer concentrations (from 0 to 20 wt%) in 1-octanol. Here PVPone was used, so that the emulsion could be prepared at room temperature. For standard emulsions – as long as the volume fractions of the dispersed phase is constant – such an addition of polymer in the
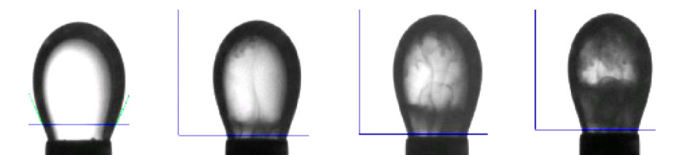

Fig. 5 Rising droplet of PVPone/1-octanol in water/PVA solution; time increases from left to right, from the droplet formation to a droplet age of 5 minutes. The drop size is 1 mm. Vertical and horizontal blue lines comes from the software we used to monitor the surface tension.
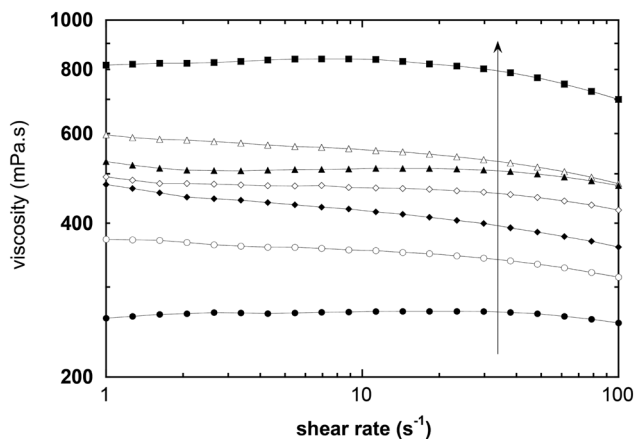
Fig. 6 Shear-rate dependence of the viscosity of the double emulsion as a function of the PVPone concentration in oil. The initial oil fraction is kept constant at 0.5. The arrow indicates the increase of the concentration of PVPone, from 0 to 20 wt%.

dispersed phase must have no impact on the emulsion viscosity, consistently with the Krieger–Dougherty law. However, we observed that the viscosity of the emulsion significantly increased when increasing the amount of PVPone in oil (Fig. 6).

This is a clear – though indirect – way of evidencing that the polymer concentration in oil sets the water transfer, which finally change the effective volume fraction and the final size of the internal droplet in oil. In the Fig. 7, we plot the viscosity (at a shear rate of 10 s^{-1}) as a function of the polymer concentration, normalized by the viscosity without PVPone: the observed non-linearity is first qualitatively consistent with a viscosity variation due to a change of the volume fractions. The next step is then to check whether this variation is quantitatively consistent with all the other measurements. In that respect, we can adjust these relative variations of the viscosity to the Krieger–Dougherty law, to determine to which variations
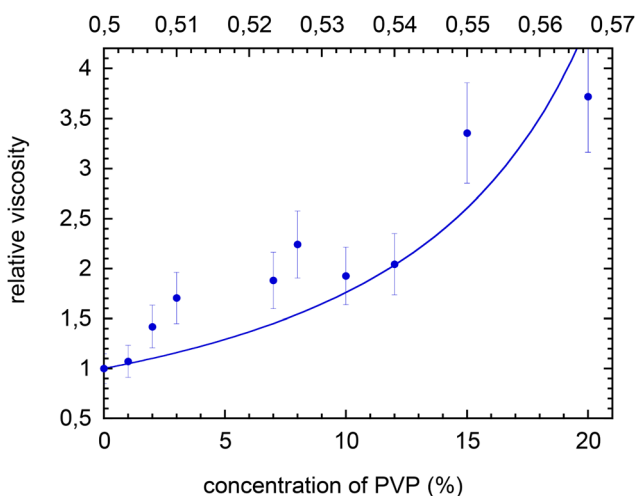

Fig. 7 Normalized viscosity of the double emulsion as a function of the PVPone concentration in oil (bottom x-axis). Once fitted by the Krieger–Dougherty law, the corresponding variations of the dispersed phase volume fraction is given on the top x-axis.

of the volume fraction of the dispersed phase such a viscosity variation corresponds. Fitting these data by the Krieger–Dougherty law (assuming $\Phi_{max} = 0.65$ and $[\eta] = 2.92$), we obtained the solid line which is associated to the top horizontal axis: thus, if the change of viscosity is generated by an increase of the effective volume fraction, such a viscosity variation actually corresponds to a volume fraction increase of about 13%, from 0.5 to about 0.57. Though this variation may look small, it turns out – using simple geometrical arguments allowing us to shift from volume fraction to droplet radius ratio - that this increase of volume fraction corresponds to the incorporation of an internal water droplet with a radius reaching 1/2 of the initial oil droplet radius, which is fully consistent with our microscopic observations (Fig. 3). Therefore, we also have a quantitative validation of the proposed mechanism of water transfer (though over a relatively small range of volume fraction, from 0.5 to 0.57).

Therefore, the variations of the emulsion viscosity well reflect the amplitude of the water transfer, set by the polymer concentration, and resulting in various volume fraction and internal droplet sizes. Other observations are consistent with this change of volume fraction induced by water diffusion. In particular, we observed that at an initial volume fraction of oil of 0.6, gels were obtained when forming the double emulsions. Such an elastic texture is not yet expected at this oil fraction, and was indeed not observed using polymer-free octanol dispersion at that same fraction of 0.6. But once polymer is added to octanol, the water transfer increases the dispersed phase volume fraction, eventually over the jamming threshold (about 0.65), and a jammed gel-like texture is thus obtained. To obtain jammed elastic double-emulsion, one can also set the initial oil fraction above 0.65. This required to use different mixing processes. Using a home-made double-syringe setup, we succeed to make emulsion with an initial oil fraction up to 0.75.[54] The resulting emulsion has then an elastic texture, very similar to the one of concentrated emulsions, with a yield stress up to 20 Pa, and a shear thinning behavior under flow.

3.4 Optimized formulation and pH-sensitive emulsion

Once the double emulsions were produced, we observed in some cases the release of the internal W1 aqueous droplet in the W2 continuous phase, leaving a 'simple' empty O/W droplet. This was confirmed by observing an emulsion after two days at rest, in which an increased amount of empty 1-octanol droplets were observed. In that respect, the stability of the inner droplet was further markedly increased by adding common emulsifiers (span 85, pluronic L61) together with PEG in 1-octanol. As well, glycerol was also successfully added to the water phase to prevent the destabilization of the emulsion. As an aside, transparent double-emulsions were obtained as the reflective index of the mixture of the water–glycerol mixture can be adjusted to match the one of 1-octanol.

Beside adding small molecular weight emulsifiers in 1-octanol, we also tested polymeric stabilizers. In particular, we produced pH responsive double emulsions by using carboxyl-end derivative of PNIPAM (poly-n-isopropyl-acrylamide): PNIPAM-COOH (MW: 10 kDa, 2–5 wt%) co-dispersed with PEG
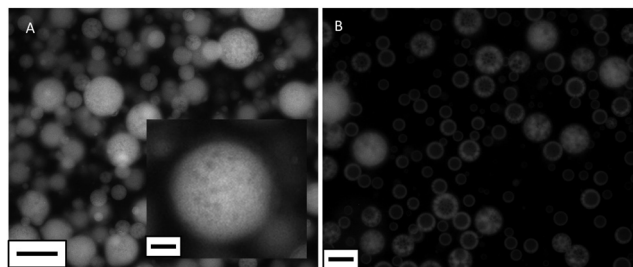
Fig. 8 Dark field microscopy images of double emulsions prepared with PNIPAM-COOH co-dispersed with PEG in 1-octanol, at (A) high pH and (B) after decreasing the pH. The scale bar is 20 μm for both images, and 5 μm for the inset A.

(10 wt%) in 1-octanol. In parallel, the pH of the continuous phase was increased with NaOH (1 M, 50 μL in 2 mL of PVA solutions) to deprotonate the PNIPAM-COOH molecules. Then, the hot oily phase was poured inside this basic aqueous PVA solution as above. The resultant emulsion showed very bright droplets by dark field microscopy with multiple smaller darker droplets within (Fig. 8A and inset). This observation suggests that multiple-core double emulsion formed in this case, and that the deprotonated PNIPAM-COO- derivative helped stabilizing many aqueous droplets within oil ones, once formed upon water diffusion.

In bulk, once produced at high pH as described above, the pH of the sample was decreased by adding HCl to re-protonate the PNIPAM-COO- derivative. The resulting double emulsion showed droplets with a very bright shell and a single dark core, suggesting that a transition from a multiple core to a single core double emulsion occurred when decreasing the pH (Fig. 8B). This feature was also nicely evidenced by decreasing the pH by adding a HCl drop on the glass microscopy slide when observing the multiple core double emulsion initially prepared at basic pH (Movies S2 and S3 in ESI†). In the first Movie (S2) (ESI†) prepared using 2 mL PVA solution, 50 μL NaOH and 200 μL octanol (containing PEG and PNIPAM-COOH as described above), the decrease of the pH induced a fast transition of many multiple core droplets into single core ones; whereas for others, the transition occurred slower, affording to observe the coalescence of internal aqueous droplets. In the second Movie (S3) (ESI†), the initial basic multiple core double emulsion was more concentrated, implying droplets in close contact, so that the decrease of the pH occurred more progressively when adding HCl on the microscopy slide (from right to left on the movie). Altogether, these experiments confirm that PNIPAM-carboxylate allows the formation and stabilization of multiple core double emulsion by using our novel method, but only when this derivative is deprotonated. Reprotonation of the derivative induces coalescence and a transition to single core double emulsion, with the inner water droplets similar to those obtained when only PEG or PVPone was initially dispersed into 1-octanol.

4 Conclusions

We report a novel and simple method to produce W1/O/W2 double emulsions, based on a dispersion of hydrosoluble polymers in oil. By a single mixing process of this oily solution with an aqueous solutions containing PVA, the mixtures transformed into a W1/O/W2 double emulsion, with the two water phases, W1 and W2 having controlled and different chemical compositions.

We showed, combining single-drop experiments, microscopy and rheology, that water diffuses from the outer continuous phase into the oily droplet, hydrating the hydrosoluble polymers present in it, and forming an aqueous droplet in the oil droplet. The process is ended once the osmotic pressures between the inner W1 droplet and the continuous W2 phase are equilibrated. As a consequence, such a mechanism allowed us to adjust the amount of transferred water by the initial polymer concentrations. In parallel, we showed that the emulsion viscosity actually depends on this transfer of water from the continuous phase to the inner water droplet.

Additionally, we observe that deprotonated PNIPAM-carboxylate co-dispersed with PEG in octanol allows the stabilization of multiple core double emulsions (also evidencing for the first time that PNIPAM-COO- molecules can actually stabilize a W/O emulsion). Moreover, these multiple core double emulsions can rapidly transform into single core double emulsion when the pH is decreased.

Double emulsions can be used as templates to produce advanced hierarchical materials; as well, they are also used in drug delivery applications or food technology for encapsulating both hydrophilic and hydrophobic cargoes. In many other fields, like cosmetics, their potential use is increasing. Still, producing controlled double emulsions remains a challenge. We believe that the findings reported here can be of interest in this research field, first because it is based on a simple process which can be used in bulk and for large volumes, and secondly because they demonstrate the efficiency of using osmose-induced diffusion effects to obtain spontaneous separation and encapsulation of the different phases.

Conflicts of interest

There are no conflicts to declare.

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