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Emulsions

Polymer-Mediated Hierarchical and Reversible Emulsion Droplet Assembly**

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Liquid emulsions—the dispersion of one liquid throughout another immiscible liquid in the form of droplets—are fundamental components of many modern products and formulations, and are useful templates for complex materials synthesis.[1–9] The liquid–liquid interface of conventional emulsions is typically stabilized by using small molecule surfactants, however these structures are only kinetically stabilized. In contrast, particles can have extremely high interfacial energies of attachment and can form stable and reproducible emulsions.[10] Providing that the surface chemistry of the particles can be tailored, particle desorption can be controlled by using external stimuli. These so-called responsive surfactants can be used to "trigger" demulsification and release the internal phase.[11–14] While responsive surfactants have academic and commercial potential, their application has been almost entirely restricted so far to that of "making and breaking" emulsions.

Herein, we report a new class of responsive polymeric surfactants that produces highly stable and functional micrometer-sized emulsion droplets. The droplet surface functionality has been designed so that reversible hydrogen-bonding interactions can be exploited to kinetically trap[2,15,16] the droplets in controlled geometries (Figure 1 a–e). Our droplet-trapping concept—referred to as "emulsion engineering"—builds on concepts used in colloidal engineering[17–19] and food science,[20–22] but employs the responsive polymeric surfactant to precisely mediate interdroplet interactions. A variety of complex liquid-based structures can be fabricated with a high degree of morphological control and uniformity. The interdroplet interactions are reversible, thus these engineered emulsions can be readily disassembled back into stable, discrete droplets by using a simple pH trigger. Control and selectivity over both the assembly and disassembly processes is demonstrated.

We have synthesized amphiphilic branched copolymer surfactants (BCSs) based on methacrylic acid (MA) and poly(ethyleneglycol) methacrylate (PEGMA) with hydrophobic dodecane chain ends.[23,24] PEGMA and MA functionalities were chosen to provide: 1) simultaneous steric and electrostatic stabilization in basic solution, and 2) the ability to form multiple hydrogen bonds under acidic conditions. MA/EG ratios of unity were initially chosen, as hydrogen bonding between these residues occurs in 1:1 stoichiometry.[11] The branched architecture ensures that each surfactant molecule contains multiple potential points of attachment to the droplet surface and dodecane chain ends were chosen to mimic the oil phase. The average polymer chain-end concentration was shown by ^{1}H NMR spectroscopy to be 11 % based on total polymer mass. An aqueous solution of BCS (2 % w/v) was prepared at pH 10, when MA is in its anionic form, and homogenized with an equal volume of dodecane[25] to produce an oil-in-water emulsion (Figure 1 f, average droplet diameter 9.2 μm, span 1.18). The emulsion creamed over several hours to give a localized oil volume fraction, Φ, of 0.68 which could be redispersed by gentle agitation. Laser diffraction measurements revealed no change in the droplet size or size distribution and no oil separation over a nine month period. In contrast, emulsions stabilized by analogous linear copolymers coalesced substantially over several weeks, presumably because of the weak droplet adhesion afforded by the single hydrophobic chain end. Emulsions prepared with the BCS and oil-soluble dyes (0.1 % w/v) had similar droplet diameters and stabilities, which demonstrates that these emulsions can encapsulate guest molecules.

An aliquot of the emulsion ($\Phi = 0.68$) was pipetted into a tapered vial and HCl was added to trigger hydrogen bonding between the protonated MA and EG residues on the droplet surfaces. Removal of the vial left a self-supporting, monolithic emulsion assembly, which conformed to the dimensions of the vial template (Figure 1 i). Successive charges of emulsions loaded with different oils produced multicomponent, layered monoliths (Figure 2 b), which could be sculpted into different self-supporting shapes. Various kinetically-trapped structures could be fabricated by employing different templates (Figure 2 a–d), however the production of very large monoliths (dimensions greater than centimeters) is limited to some extent by diffusion of acid throughout the structure. All engineered emulsions retained their structural integrity upon storage in HCl (1 M) for at least four months.

Disassembly of the engineered emulsions was assessed by raising the pH of the continuous phase. In all cases, the trapped structures disassembled back into conventional, dispersed, and noninteracting emulsion droplets. This base-triggered disassembly was driven by simultaneous hydrogen-bond decomplexation and electrostatic repulsion of the anionic PMA residues (p$K_a \approx 5$) on the droplet surfaces and was extremely rapid (< 1 min for the monolith dissociation shown in Figure 1 i, j). Light microscopy and laser diffraction

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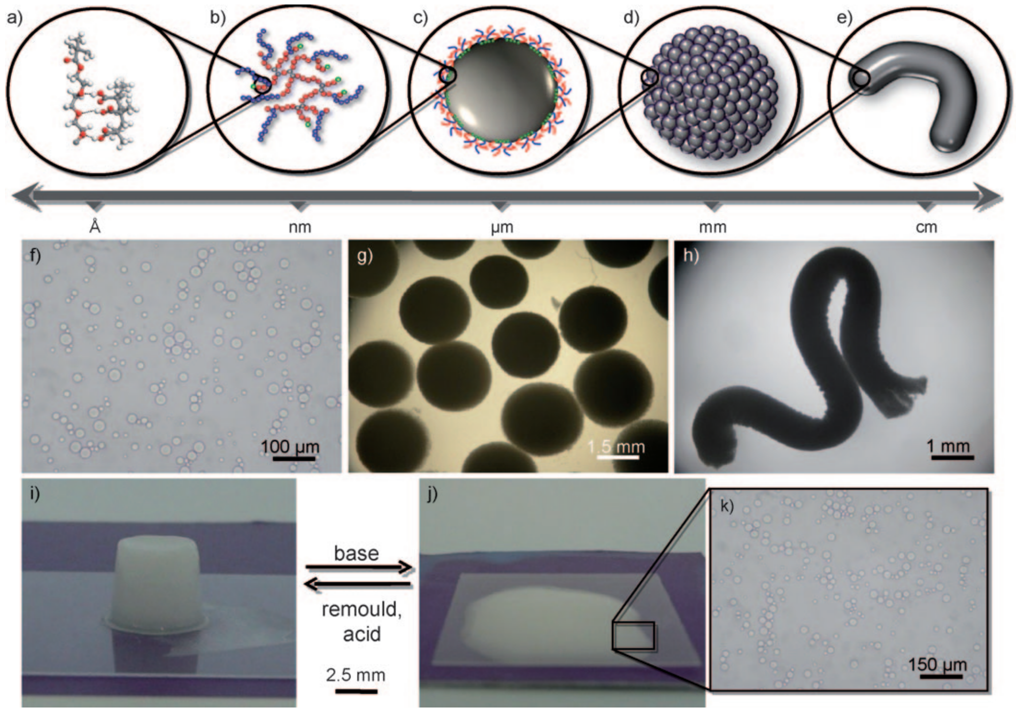

Figure 1. a–e) Reversible hierarchical emulsion droplet assembly; f) light micrograph of dispersed emulsion droplets at high pH; g) "spheroidal" assemblies; h) assembled "fiber"; i) templated monolithic assembly; j) disassembled monolith in (i) 1 min after addition of base; k) light micrograph of (j).

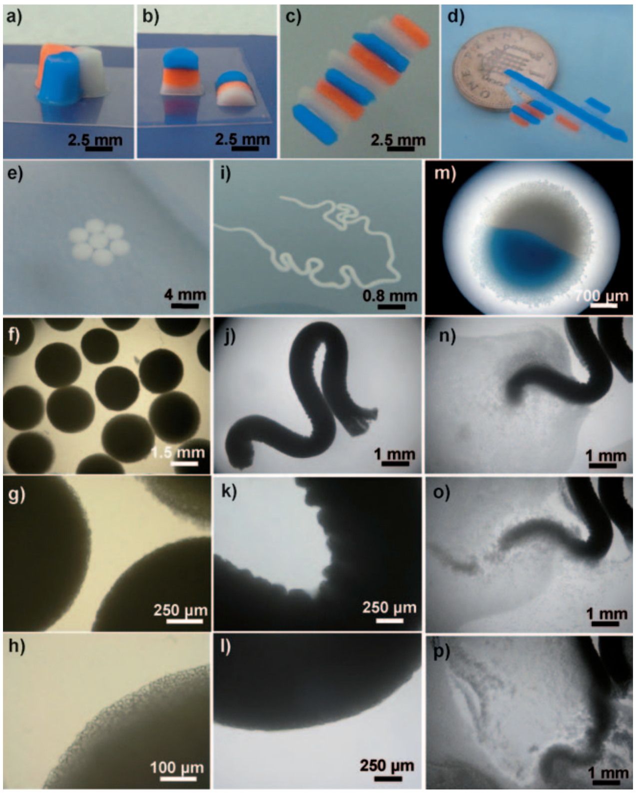

Figure 2. Images of engineered emulsions. a–d) templated emulsion assemblies; e–h) spheroidal assemblies at increasing resolution; i–l) fiber assemblies at different resolutions; m) macro-Janus assembly; n–p) pH-triggered disassembly of assembled fiber (j). Images were recorded at 3 s intervals.

confirmed the individual emulsion droplets retained their structural integrity and no demulsification was observed after disassembly (a video of emulsion engineering assembly and disassembly processes is available in the Supporting Information).

Alternative emulsion engineering strategies were investigated with scale-up and automated preparation in mind. Aliquots of the emulsion were successively dripped into aqueous acid using a micropipette. Spheroidal engineered emulsions with narrow size distributions (< 5 %) were readily obtained (Figure 2 e–h), providing that the oil volume fraction exceeded 0.48 and the HCl concentration was above 1 mM (see the Supporting Information). Spheroids were produced as the liquid emulsion minimized its surface area and rapid hydrogen-bond formation ensured that the structures were trapped in these confinement geometries.[26] Spheroid diameters were dictated by the volume of emulsion dripped into the acid. The smaller dimensions of these structures allowed more intimate structural interrogation and confirmed the presence of close-packed, discrete, and disordered emulsion droplets (Figure 2 f–h). Simultaneous dripping of dye-loaded (blue) and nondyed (white) emulsions into aqueous acid produced "macro-Janus" spheroids with distinct hemispheres (Figure 2 m). In principle, anisotropic macro-Janus assemblies could be produced by varying the volumes of the white and blue emulsions. No intermingling of the hemispheres was observed over several days, which indicates high encapsulation efficiencies and negligible interdroplet dye diffusion. Fiber morphologies were produced by extruding the emulsion below the surface of acidic water from a needle; these were stabilized by the rapid formation of hydrogen bonds between adjacent droplets (Figure 2i–l). Fiber diameters could be controlled by varying the needle diameter and dispensing rate, and fiber lengths were limited only by the volume of emulsion that could be dispensed in a continuous fashion: this could be increased (in principle without limit) by using continuous injection methods. Interdroplet hydrogen-bonding interactions within bent fibers caused the inside of the bend to buckle under compression; conversely, the external bend formed a smooth surface under tension (Figure 2j–l), which implies these engineered emulsions have some mechanical strength. Again, base addition triggered rapid disassembly (Figure 2n–p) and dripping or extruding the emulsions into aqueous base produced stable emulsion dispersions.

We investigated whether the droplet assembly process could be controlled using the composition of BCS. Emulsions stabilized with an analogous BCS comprising an excess of EG residues (MA/EG 1:2) was prepared. The droplet diameters of both emulsions were monitored by laser diffraction as a function of time under different conditions (represented as zones 1–4 in Figure 3e, f). In basic solution, both the MA/EG 1:1 and 1:2 emulsions were efficiently dispersed (Figure 3b and d) because of simultaneous steric and electrostatic stabilization, as evidenced by constant droplet diameters in zone 1. Upon lowering the pH of the solution, the MA/EG 1:1 droplets assembled (shown as increasing droplet diameters in Figure 3e, zone 2), however, the MA/EG 1:2 BCS-stabilized droplets remained completely dispersed (constant droplet diameters). In the case of the MA/EG 1:2 droplets at low pH, the MA residues hydrogen bond with available EG residues around the same droplet, however hydrogen bonding between droplets is prevented because of the steric contributions of the additional PEGMA residues (Figure 3c). Thus the intra- versus interdroplet hydrogen bonding interactions can be controlled for these emulsions (see the Supporting Information). A similar mechanism operates during the electrostatic shell cross-linking of block copolymer micelles where intermicellar cross-linking can be prevented when an additional steric-stabilizing block is present on the micelle periphery.[27]

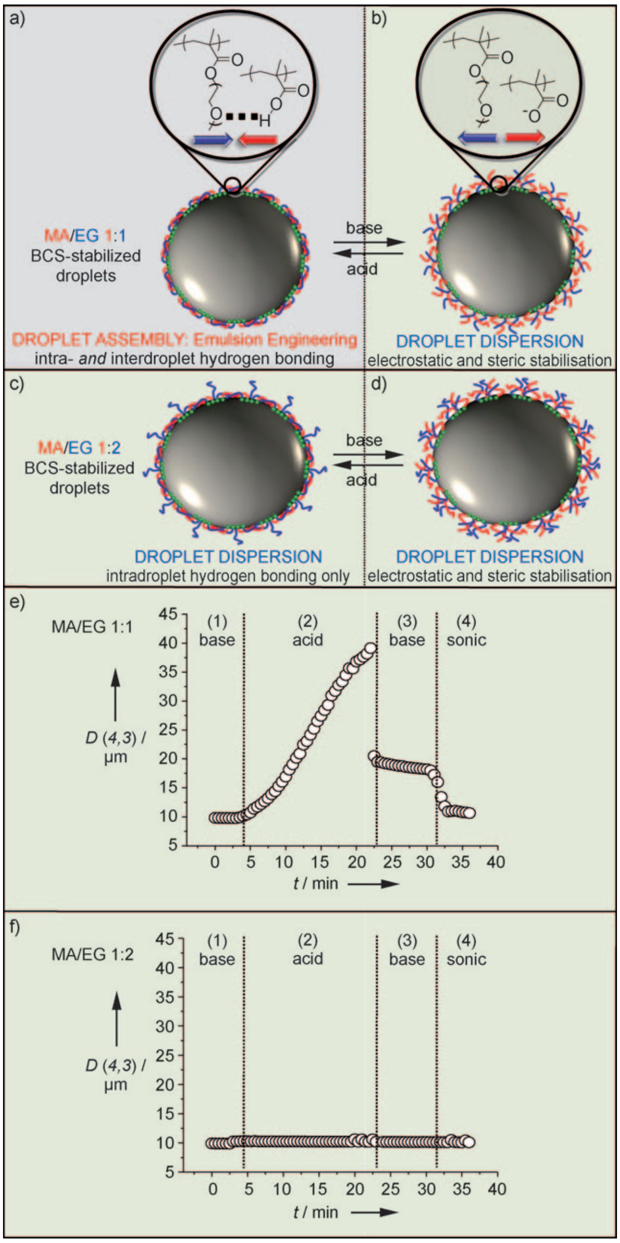

Figure 3. Effect of BCS composition on interdroplet interaction potentials. a) intra- and interdroplet hydrogen bonding occurs at low pH for MA/EG 1:1 droplets, which causes interdroplet attraction and assembly; c) excess steric stabilization from MA/EG 1:2 droplets prevents interdroplet hydrogen bonding, interdroplet repulsion predominates at low pH; b, d) steric and electrostatic stabilization occurs at basic pH, thus interdroplet repulsion predominates in both cases. Average droplet diameters, $D(4,3)$, of e) MA/EG 1:1 and f) MA/EG 1:2 droplets under various conditions: 1) pH 9, 2) reducing the pH value of the solution to 2, 3) increasing the pH value of the solution to 11, and 4) gentle sonication at pH 11.

Having demonstrated control over the assembly process, we investigated the possibility of controlling the disassembly process since this would be highly desirable for controlled release applications. Macro-Janus spheroids were kinetically trapped by using MA/EG 1:1 BCS at 40 °C in aqueous acid. In contrast to previous emulsion assemblies, one of the hemispheres comprised an internal phase of 1-dodecanol (dyed blue for clarity) which crystallizes below its melting point (ca. 24 °C), and the other hemisphere comprised dodecane (white). The engineered structures were cooled to 20 °C, whereby the blue hemisphere (lower hemisphere in Figure 4a) underwent an additional thermal-trapping process, as the oil crystallized when the droplets became nonspherical[28] (see the Supporting Information). In principle, each hemisphere of these macro-Janus spheroids could be disassembled in turn by using a pH trigger followed by a thermal trigger.[28] On raising the pH of the solution, the white hemisphere that comprises "conventional" spherical dodecane droplets rapidly disassembled (Figure 4b–e), to leave the thermally-trapped 1-dodecanol hemisphere intact because of the nonspherical droplet morphologies (Figure 4f). Increasing the solution temperature above the melting point of 1-dodecanol at basic pH reformed spherical droplets, which rapidly disassembled (Figure 4g–j). Minor demulsification was observed on heating (note two macroscopic droplets in

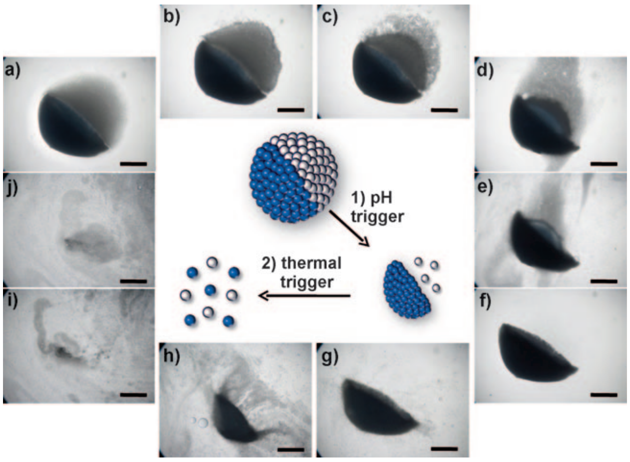

Figure 4. Selective disassembly of macro-Janus droplet assemblies. a–e) Trigger 1: pH-induced disassembly at 5 s intervals. f) Thermally-trapped hemisphere at pH 9 and 20 °C. g–j) Trigger 2: thermally-induced disassembly of 1-dodecanol hemisphere on heating at 7 s intervals. Scale bars: 1 mm.

Figure 4 h), which indicates these 1-dodecanol droplets are not entirely tolerant of temperature fluctuations.

In summary, we have demonstrated a convenient new strategy to reversibly assemble stable functional emulsion droplets into robust liquid structures. The assembly and disassembly process is driven solely by interactions on the droplet surface, which can be controlled by subtle variation of the BCS composition. Engineered emulsions have far-reaching potential in applications where encapsulation and controlled delivery of large payloads is desirable.

Experimental Section

Synthesis of MAA/EG 1:1 BCS: A mixture of PEGMA (6.732 g, 6 mM), MAA (10.000 g, 116 mM), ethyleneglycol dimethacrylate (EGDMA, 2.302 g, 12 mM), and 1-dodecanethiol (0.474 g, 12 mM) was degassed. Ethanol (190 mL) was degassed separately and added to the monomer mixture. After heating to 70 °C, the polymerization was initiated by addition of AIBN (190 mg) and was left stirring for 48 h. Ethanol was then removed by distillation and the polymer was washed with cold diethyl ether and dried. ^{1}H NMR confirmed that the chemical composition was in good agreement with monomer feed ratios. The synthesis of MAA/EG 1:2 BCS was identical, however the molar equivalents of PEGMA to MAA were altered accordingly. Synthesis of linear copolymers was identical, however EGDMA was omitted and only 2 molar equivalents of 1-dodecanethiol were used.

For the preparation of emulsions, aqueous polymer solutions (2.0 wt %, pH 10) were homogenized with an equal volume of oil at 24 000 rpm for 2 min. All emulsions were characterized by laser diffraction.

The Supporting Information includes characterization of copolymers and emulsions and further emulsion engineering demonstrations.

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