

Moldable high internal phase emulsion hydrogel objects from non-covalently crosslinked poly(*N*-isopropylacrylamide) nanogel dispersions†

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High Internal Phase Emulsion hydrogels are prepared from water-borne poly(*N*-isopropylacrylamide) nanogel dispersions which are non-covalently crosslinked through 2-ureido-4[1*H*] pyrimidinone (UPy) quadruple hydrogen bond groups. The reversible UPy cross-links allow for the HIPE-hydrogels to be molded into objects which are thermo-responsive in nature.

Assembly of colloidal objects into larger macroscopic supracolloidal structures can lead to fascinating materials with applications spanning across a breadth of scientific disciplines. Interesting soft colloidal materials can be made using emulsion droplets as building blocks. Pickering described the fabrication of oil-in-water high internal phase emulsions (HIPE) using soap with oil volumes of up to 99% in 1907.¹ He reported that the resulting oil-in-water emulsions became practically solid, resembling a blancmange. A jammed state of the emulsion droplets provides the HIPE with a yield stress, allowing HIPEs to maintain specific shapes. We previously showed that this quiescent emulsion behaviour can be used to fabricate arrested “banana-shaped” HIPE droplets using a microfluidic flow-focussing device.² Low-shear quiescent emulsion technology can also be accomplished through gel-formation of the continuous phase by other means, as for example illustrated by our recent work on fruit-juice infused chocolate confectionary.³ A combination of fumed silica particles and chitosan is used to achieve both Pickering stabilization, that is emulsion droplets stabilized by solid particles, and the formation of a continuous gel phase with a yield stress (that is at low shear) in the molten stage. Non-covalent interplay between fumed silica particles and chitosan underpins both phenomena. The concept of organizing emulsion droplets into a reversible gel-like matrix making use of secondary interactions has been beautifully developed by Weaver and co-workers, the process coined “emulsion engineering”.⁴ They made use of polymeric stabilizers present on the surface of the droplets that have the ability

to undergo reversible hydrogen bond interactions, hereby locking the droplets together into a soft supracolloidal structure whilst preserving droplet identity. Ngai showed that oil-in-water HIPE-gel structures with internal phase of up to 90% can be prepared using a waterborne dispersion of poly((*N*-isopropylacrylamide)-*co*-(methacrylic acid)) microgels.⁵ They suggest that the hydrogel-like continuous phase is formed as a result of hydrogen bond interactions. Ngai extended his approach to fabricate HIPE-gels by using core-shell particles, that is polystyrene particles with an outer shell of microgel copolymer.⁶ Recently, we showed that HIPE-organogels could be made under low shear force by using soft poly((methyl methacrylate)-*co*-poly(butyl acrylate)) latex particles which were functionalized with a small amount of 2-ureido-4[1*H*] pyrimidinone (UPy).⁷ UPy units can undergo very strong and highly directional self-complimentary quadruple hydrogen bonding through their dimerization, as first reported by Meijer and co-workers.⁸ Upon contact with the oil phase the polymer chains in the particles unravel due to swelling, which leads to the formation of the organogel. The HIPE-organogel is physically reinforced through the multiple hydrogen bond interaction of the UPy moieties and the structures are able to withstand a large osmotic pressure gradient. Use and removal of a volatile oil phase led to the formation of a closed-cell bubble wrap-type structure, with water (instead of air bubble) compartments.

Herein we report the fabrication of HIPE-hydrogels using poly(*N*-isopropyl acrylamide) (pNIPAm) nanogels which are non-covalently crosslinked through UPy quadruple hydrogen bond interactions, that is through reversible formation of UPy dimers acting as physical crosslinks.⁹ We demonstrate that the HIPE-hydrogels can be shaped into reconfigurable shaped objects by means of injection molding. Moreover, the lower critical solution temperature (LCST) character of the pNIPAm allows the structures to be shrunk substantially at elevated temperatures allowing for triggered release of guest molecules.

Waterborne pNIPAm nanogels non-covalently crosslinked through UPy hydrogen bond interactions were prepared by precipitation polymerization. Note that no bisacrylamide was used. The polymer chains forming the nanogel particle (being crosslinked, branched and linear) are held together by reversible

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UPy dimerization, warranting the identity of the particle, even in water. DLS measurements at 25 °C showed the existence of swollen microgel particles with an average diameter of 161.3 nm (NGP3).⁹ When particles are brought into contact with each other for prolonged time periods the polymer chains can rearrange, effectively fusing the colloids together. This self-healing capability makes the nanogels ideal candidates for the preparation of moldable high internal phase emulsion (HIPE) hydrogels. One key difference with the HIPE-gels made by Ngai *et al.*⁵ from poly((*N*-isopropylacrylamide)-*co*-(methacrylic acid)) microgels is that ours can be reshaped and thus structurally relaxed on a polymer chain level, whereas theirs being covalently crosslinked only allow for interparticle rearrangement upon deformation. Oil-in-water HIPE-hydrogels were designed with an internal hexane phase volume of 80%. They were simply prepared by shearing a mixture of hexane (dispersed phase) and a dilute aqueous dispersion of nanogel particles, down to 0.5 wt% (Fig. 1a). Self-supporting HIPE-hydrogels were formed immediately even at this low solid content of nanogel particles (Fig. 1b). Upon shearing the particles initially act as Pickering stabilizers, meaning that they adhere to the hexane droplet interface. Rearrangement of the polymer chains can occur as a result of the reversibility of the UPy dimerization, allowing for the structure formation and reinforcement of the hydrogel continuous phase. The HIPE-hydrogel adheres to the glass vial and has a sufficiently high yield stress (not to flow) under its own gravitational force. Confocal laser scanning microscopy (CLSM) was used to observe the microstructure of the HIPE-hydrogels. For this, the nanogel particles were fluorescently labeled through copolymerization of small quantities of Rhodamine B piperazine methacrylamide. A hostasol dye was loaded in the hexane dispersed phase. Fig. 1d, e and f confirm that oil-in-water (O/W) HIPE-hydrogels were formed, with hexane droplets entrapped into the aqueous continuous gel-phase. The droplets have a size range from several micrometers to ~60 μ m.

Exposure of a small sample of the HIPE-hydrogels to the open atmosphere led to preferential evaporation of the more volatile hexane, hereby deforming the spherical structure of

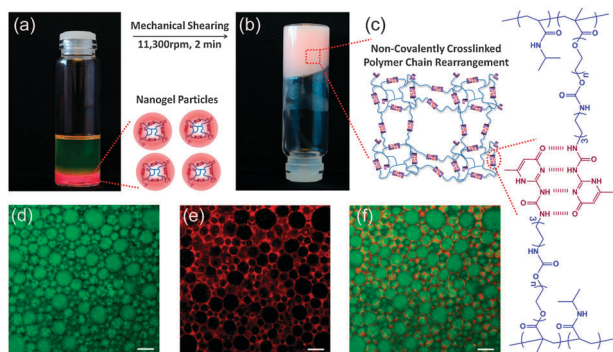


Fig. 1 (a) 2.4 ml of hostasol fluorescent dye loaded hexane (green top) and 0.6 ml of Rhodamine B labelled nanogel particles (0.5 wt%, pink bottom) before emulsification; (b) appearance of the oil-in-water HIPE-hydrogel; (c) schematics of the structure of HIPE-hydrogel; (d) confocal image of the oil-in-water HIPE-hydrogel, excited by laser with a wavelength of 488 nm for the hostasol dye; (e) confocal image of the fluorescently tagged HIPE-gel, excited by laser with a wavelength of 514 nm; (f) the combination of the two channels; scale bars: 50 μ m.

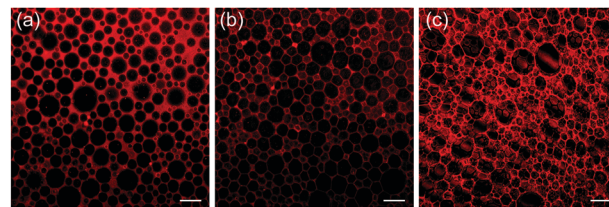


Fig. 2 Confocal images of the HIPE-hydrogels made from Rhodamine labeled nanogels. (a) Freshly made wet state; (b) after drying in air for a few minutes; (c) after 30 min, majority of both liquid phases was evaporated, scale bars: 50 μ m.

droplets into a polyhedral morphology. After prolonged drying periods (30 min), the majority of both liquid phases had evaporated, leaving a bubblewrap-type monolithic foam, as clearly can be seen in Fig. 2c. Note that no fusion of neighboring cells was observed during the drying periods, preserving a closed-cellular structure (see also Fig. S1 (ESI[†]) for SEM analysis of dried HIPE-hydrogels made using different concentration of nanogel particles). Increasing the amount of the nanogel particles did not result in an apparent variation of pore size and thus droplet size, which means that at this concentration range the emulsion droplet size was determined by the amount of shear. However, upon increasing the nanogel concentration, the skeleton of the polymeric foam formed is structurally more solid and is capable of withstanding its own weight comfortably. Thin, partially ruptured polymeric films covering the pore windows can be found in the samples due to the rupturing of the cells when exposed to vacuum. Similar phenomenon has also been observed in Pickering polyHIPEs.¹⁰

The mechanical properties of the HIPE-hydrogels were investigated by rheological measurements. Fig. 3 shows the dependence of the storage and loss moduli of HIPE-gels on frequency in the oscillatory frequency sweep. Throughout the frequency range, the storage modulus (G') is always considerably higher than the loss modulus (G''), which indicates that stable HIPE-gels were formed. In addition, as we expect, the storage modulus of the HIPE-gels increases with the increased loading of nanogel particles, which means the more particles added the higher mechanical strength will be obtained. However, the storage modulus of the HIPE-gels with 5 wt% of particles is not significantly higher than the sample with 2 wt%. The possible reason is that the excess nanogels particles still disperse in the water phase rather than stick to droplet interface to help forming a thicker and stronger nanogel network.

Macroscopic hydrogel structures which have been crosslinked through covalent interactions have a permanent shape. The inability for such hydrogels to self-heal and undergo flow makes re-shaping through for example injection molding not possible. In contrast, our HIPE-hydrogels have a non-permanent reversible gel structure, as the network is formed through non-covalent crosslink points. This means the gels will have a yield stress above which flow and thus shape re-molding can occur (Fig. 4).

To demonstrate this we injection-molded our HIPE-gels into plastic micropipette tips as templates. The hexane droplets were occasionally labeled with different dyes to ease observation. Self-standing HIPE-hydrogels of the shape of the template were easily obtained (2 wt% of nanogel dispersion used). Injection of a layer of non-labelled and a subsequent layer of

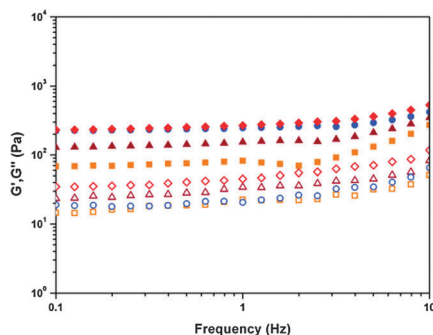


Fig. 3 Storage modulus G' (closed symbols) and loss modulus G'' (open symbols) of HIPE-hydrogels with different loading amounts of nanogel particles (yellow: 0.5 wt%, purple: 1 wt%, blue: 2 wt%, red: 5 wt%) as a function of frequency in the oscillatory frequency sweep.

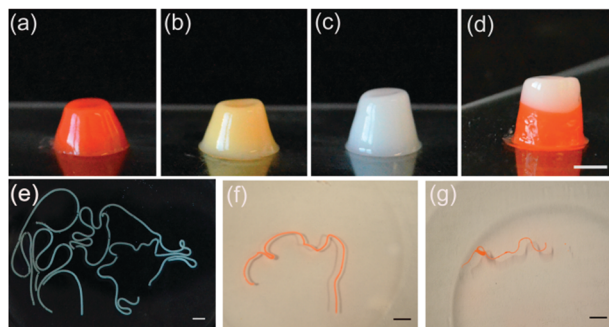


Fig. 4 (a–c) Remolded coloured HIPE hydrogel monoliths; (d) two-zone HIPE hydrogel, (a–d) scale bar: 2.5 mm; (e) emulsion gel fibers generated via syringe injection; (f) fiber with dye loaded at room temperature 20 °C; (g) after heating up to 60 °C, (e–g) scale bars: 5 mm.

labeled gel into the microtip mold led to the formation of a two-zone HIPE-hydrogel structure, which maintained its characteristics (Fig. 4d). The sharp distinction between the red labeled and the unlabeled zone proves that hexane droplets are trapped into the continuous hydrogel matrix (the image was taken after 10 minutes; one could speak of a quiescent high internal phase emulsion). Moreover, it proves that the HIPE-hydrogel morphology is one of closed-cellular structure, as an open-cell structure (that is with interconnectivity between the droplets) would cause rapid diffusion of the red dye over the entire hexane phase.

The ability to flow at higher stress allows for the fabrication of HIPE-hydrogel fibers. For this a HIPE-hydrogel was placed into a plastic syringe and injected into hexadecane oil. When gel-fibers were made from HIPE-hydrogels in which the hexane phase was labeled with Sudan III, no fast release of dye into the hexadecane liquid from the fibers was observed, again supporting a closed-cell morphology. The HIPE-hydrogel fibers are scaffolded by the thermoresponsive pNIPAm. When we heat the fiber which was immersed in hexadecane oil at 60 °C for 5 min, the fiber shrunk immediately due to the hydrophobic collapse of the pNIPAm polymer chains above their LCST (Fig. 4g). This resulted in a small burst release of dye. The decreased volume ratio of the fiber is around 5.72

(length ratio: $l_{lt}/l_{ht} = 1.89$, diameter ratio: $d_{lt}/d_{ht} = 1.74$, lt: low temperature, ht: high temperature), which demonstrates the excellent thermo-responsive property of the HIPE-hydrogel.

One might wonder how to conveniently produce a fully interconnected and thus open cellular structure of our HIPE-hydrogels. We found that “freeze-drying” provided a way to realize this. Fig. S2 (ESI[†]) shows the inside morphology of a freeze-dried HIPE-hydrogel, in which holes in the cellular walls can clearly be observed. We briefly investigated the release profile of entrapped and precipitated guest molecules from these interconnected macroporous monolith. Fig. S3 (ESI[†]) shows the release profile of Sudan III dye under different temperature cycles as studied by UV-Vis. In the first 30 min at ambient room temperature, Sudan III diffuses out slowly as a nanoprecipitate. After heating the system upto 50 °C (above the LCST temperature) for 2 minutes, a large quantity of Sudan dye was released, clearly shows the thermo-responsiveness of HIPE-hydrogels.

In summary, by using non-covalently crosslinked pNIPAm nanogel particles as stabilizers, we are able to prepare HIPE-hydrogels. The HIPE-hydrogels can be remoulded into desired shapes and exhibit excellent thermo-responsive properties. The mechanical strength of the HIPE gels can be tuned by varying the amount of nanogel particles used. We believe that these remoldable and thermoresponsive HIPE-hydrogels open up exciting areas in soft matter science, for example their use as responsive sponges for the storage, transport and delivery of active (colloidal) substances.

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