Bio-Inspired Self-Healing Capsules: Delivery Vehicles and Beyond

*Gianluca Etienne, Esther Amstad**

G. Etienne, Prof. E. Amstad
Soft Materials Laboratory, Institute of Materials, École Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland
E-mail: esther.amstad@epfl.ch

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(Microcapsules are often used as individually dispersed carriers of active ingredients to prolong their shelf life or to protect premature reactions with substances contained in the surrounding. Here, we go beyond this application and employ microcapsules as principal building blocks of macroscopic 3D materials with well-defined granular structures. To achieve this goal and inspired by nature, we fabricate capsules from surfactants that are functionalized with catechols, a metal-coordinating motive. These surfactants self-assemble at the surface of emulsion drops where they are ionically crosslinked to form viscoelastic individually dispersed capsules that display a low permeability even towards small encapsulants. However, due to their high affinity to each other, the use of capsules is not limited to carriers: We go a step beyond the current use of capsules and demonstrate that these sticky capsules are well-suited building blocks of additive manufactured granular structures. Thereby, they open up new opportunities for additive manufacturing of soft, self-healing materials composed of individual compartments that can be functionalized with different types of spatially separated reagents.)

1. Introduction

Polymer microcapsules are often used as individually dispersed carriers to control the timing and location of the release of active ingredients[1] for example in food,[2,3] cosmetic,[4,5] and pharmaceutical[6,7] applications. Key to a successful application of these capsules is a good control over their mechanical stability and permeability.[8] These parameters can be tuned

with the composition and dimensions of the capsule shells. Capsules composed of thin polymeric shells that display a low permeability towards charged encapsulants are frequently made through layer-by-layer deposition of oppositely charged polyelectrolytes onto solid cores that are subsequently dissolved.[9–12] To reduce the number of deposition steps, capsules have been fabricated from covalently or ionically crosslinked reagents including polydopamines[13] and tannic acid.[14,15] The solid particle templates offer a good control over the size of the capsules. However, they limit the amount of encapsulants that can be loaded into the capsule core. This limitation can be overcome if emulsion drops are employed as templates. Indeed, capsules composed of a wide range of materials have been produced from double emulsion templates by solidifying their shells.[16,17] The flexibility in the materials choice enables the fabrication of capsules that offer triggered release of encapsulants in response to various stimuli, including changes in temperature,[18] pH,[19,20] ionic strength,[21] oil composition,[16] and the presence of enzymes.[22] However, the resulting capsules typically have rather thick shells, rendering them stiff. Their stiffness hampers their flow through narrow orifices, which would be required if they constitute the main ingredient of 3D printable inks. Moreover, the high volume fraction occupied by the shell limits the amount of encapsulants that can be loaded into their core. Feasibility to use double emulsions as templates to produce capsules with thin polymeric shells occupying less than 2% of the capsule volume has been shown.[23] However, these capsules were rather stiff such that they broke if mechanically deformed, hampering their further processing into macroscopic materials. Capsules with much thinner, flexible shells that can be loaded with significantly higher quantities of encapsulants can be fabricated if reagents are solidified at the drop surface. This can be achieved, if different types of appropriate reagents are dispersed in the drop and the continuous phase respectively and meet at the drop surface where they react through polymerization[24–26] or coacervation reactions.[27],[28] Similarly, polyelectrolyte multilayer-based capsules can be assembled from emulsion drops if they are stabilized with

charged surfactants and dispersed in a solution containing oppositely charged reagents.[29,30] Capsules with thin shells can also be produced from chemically reactive surfactants that are directly crosslinked at the drop surface.[31–35] However, the number of reagents that can be employed to form thin polymeric capsules through these approaches is limited. Flexible capsules that display a narrow size distribution, low permeability towards encapsulants, allow controlled repetitive exchanges of reagents and are mechanically sufficiently stable to withstand significant shear stresses such that they can be processed into macroscopic materials through additive manufacturing techniques remain to be established. These capsules would open up a new field of their use as principal building blocks of macroscopic materials with well-defined structures and locally varying compositions that goes far beyond their current use as individually dispersed delivery vehicles.

Here, we introduce a new type of viscoelastic, mechanically stable capsules that are composed of bio-inspired ionically crosslinked catechol-functionalized block copolymer surfactants. Because of the viscoelastic properties, capsules are self-healing such that they can be merged and split at will. These capsules present a high concentration of Fe^{3+} complexed catechols at their surface such that they have a high affinity to each other. Therefore, they cannot only be used as individually dispersed mobile carrier vehicles that display a low permeability even towards small encapsulants, but also as principal building blocks of macroscopic soft materials. We demonstrate for the first time that these capsules are mechanically sufficiently stable to serve as principal building blocks of inks that can be 3D printed into macroscopic granular materials with well-defined structures.

2. Results

Emulsion drops are often stabilized with polymeric surfactants that are crucial during drop production and storage. However, once the drops are converted into capsules, surfactants are usually superfluous or even devastating because they irreproducibly change the surface

wettability of the capsules. Instead of identifying protocols that efficiently remove surfactants from the capsule surface, we introduce surfactants that serve as building blocks to form viscoelastic capsules. To achieve this goal, we synthesize a new amphiphilic block copolymer surfactant that is end-functionalized with catechol, a metal-coordinating motive, as shown in **Figure 1a**. We employ a diblock copolymer surfactant composed of a perfluoropolyether block that is covalently linked to a poly(ethylene glycol) (PEG)-based block as a model surfactant; this surfactant has proven to efficiently stabilize water in perfluorinated oil drops.[36] To enable the formation of metal-coordination bonds between adjacent surfactants, we functionalize their PEG-ends with catechol, a molecule that forms strong complexes with certain metal ions such as Fe^{3+},[37–39] as shown schematically in **Figures 1b and c**.

To test if we can convert emulsion drops stabilized with our catechol-functionalized surfactants into viscoelastic shells, we form perfluorinated drops using a pendant drop set-up. Fluorinated drops encompassing 2 mM of the catechol-functionalized surfactant FSHPEG900HA are formed in an aqueous solution containing 1 mM $FeCl_3$. We expect catechol-Fe^{3+} complexes to form if the pH is increased to basic values where catechols are deprotonated.[38] Indeed, under basic conditions, we observe the formation of thin solid shells at the drop surface within 30 s. These shells buckle if liquid is retracted, as exemplified in the time lapse micrographs in **Figure 2a** and **Movie S1**. A similar behaviour is observed if drops are stabilized with 2 mM FSHDopa that lacks the PEG-based block, indicating that shells form even in the absence of any hydrophilic spacer, as shown in the **Supporting Figure S1a**. By contrast, if the pH is adjusted to 3, where the hydroxyl groups of catechols are protonated, we cannot observe any sign of a shell, even if the liquid is completely retracted from the drop, as shown in **Figure 2b**. Similarly, no signs of a shell formation are observed within the investigated timeframe if drops do not encompass any surfactants, as shown in **Figures 2c**, or if catechol-free surfactants are used, as detailed in the Supporting Information. These results suggest that catechol-functionalized amphiphilic block copolymers can indeed be converted

into thin shells if catechols are deprotonated such that they form multivalent complexes with Fe^{3+}.

Our results indicate that perfluorinated surfactants can be converted into viscoelastic shells if they are functionalized with catechols and ionically crosslinked. To test the generality of our approach, we synthesize a non-fluorinated, hydrocarbon-based surfactant composed of polypropylene glycol whose two ends are functionalized with catechols (DiDopaPPG), as shown in **Figure 2d**. We form toluene drops encompassing 2 mM of DiDopaPPG and 1 mM Fe^{3+} in an aqueous solution and increase the pH of the surrounding aqueous phase. Also, in this case, we observe the formation of a thin shell at the drop surface that starts buckling if fluid is retracted, as shown in Figure 2d. A similar behaviour is observed for drops stabilized with dopamine-functionalized stearic acid (SADopa), as shown in the **Supporting Figure S1c**. These results indicate that the formation of viscoelastic shells is not limited to fluorinated surfactants but also occurs if hydrocarbon-based catechol-functionalized surfactants are employed. To assess if catechol-functionalized surfactants are indeed ionically crosslinked, we perform UV-VIS spectroscopy on SADopa that is dissolved in ethanol. In the absence of any Fe^{3+} ions, an absorption peak at 280 nm, typical for catechols, is observed. Upon addition of Fe^{3+} the absorption peak shifts to 246 nm, as shown in the **Supporting Figure S2**. These results indicate that catechol-functionalized surfactants are ionically crosslinked at the drop surface.

If catechols are ionically crosslinked, the capsules should display a viscoelastic behaviour, by analogy to the catechol-functionalized hydrogels that are crosslinked with Fe^{3+} ions.[38,40,41] In this case, we expect them to merge if they are in contact with each other. To test this expectation, we form a drop composed of HFE-7100 containing 2 mM FSHDopa and 0.6 mM Fe^{3+} in a basic aqueous solution (pH = 8.5). We deposit this drop on a glass substrate and form a second fluorinated drop that is attached to a steel needle. When the two drops come in contact, they strongly adhere to each other, as shown in **Figure 3a** and **Movie S2**. If the shells

are elastic, we expect the two drops to remain intact even if the they are in contact with each other. By contrast, if the shells are viscoelastic, we expect them to merge such that reagents can be exchanged between the two drops. To qualitatively assess the mechanical properties of these shells, we form a first fluorinated drop that encompasses a 1.5 mm diameter air bubble and deposit it on a substrate. When a second drop is brought in contact with the first one, a connecting neck forms whose diameter grows until it reaches values similar to the diameter of the air bubble. At this stage, the air bubble starts raising into the pendant drop indicating that the two shells merge to form a connecting neck, as shown in the time-lapse micrographs in **Figure 3b** and **Movie S3**. These results demonstrate that the shells are viscoelastic. As a result of the viscoelastic behaviour, the two merged drops can be separated after the air bubble is exchanged, resulting in two separate intact capsules, as shown in the last two frames in **Figure 3b**. This behaviour opens up new possibilities to controllably and repetitively exchange reagents between capsules without compromising their integrity.

A key requirement for a good performance of capsules is a high mechanical stability. We expect ionic bonds to increase the stability of capsules against rupture. To test this expectation, we centrifuge ionically crosslinked capsules at 13500g. We do not observe any significant rupture or merging, indicating that these capsules are mechanically at least as stable as emulsion drops coated with optimized unfunctionalized surfactants.[36] To test the stability of capsules against rupture if dried, we produce water drops that encompass fluorescein. To closely control the size of the drops, they are formed in polydimethylsiloxane (PDMS)-based microfluidic flow focusing devices. Drops with a diameter of 114 μm are deposited onto an aqueous solution containing 0.6 mM Fe^{3+} that is buffered to pH = 8.5 using BICINE. Drops stabilized with the catechol-functionalized FSHPEG900HA surfactant self-assemble into a hexagonal close-packed monolayer. Interestingly, individual capsules with aqueous cores do not coalesce although they are in direct contact with their neighbours and they retain their integrity even if the surrounding oil is evaporated, as shown in **Figure 4a** and

Movie S4. By contrast, drops stabilized with unfunctionalized FSH-Jeffamine2000 surfactants rupture during oil evaporation, thereby releasing fluorescein to the surrounding, as shown in **Figure 4b** and Movie S4. These results indicate that the stability of emulsion drops increases upon ionic crosslinking.

The vast majority of emulsion drops are stabilized with polymeric surfactants. These surfactants typically impart stability to emulsion drops. However, they come at an important expense: Free surfactants spontaneously form micelles and small aqueous drops that carry reagents across oil phases, resulting in cross-contaminations between different drops.[42–48] This cross-contamination limits the use of surfactant-stabilized emulsion drops as picoliter-sized vessels for conducting sensitive high-throughput screening assays. This reagent transport also reduces the encapsulation efficiency if such drops are used as templates to form capsules. We expect this reagent exchange to be delayed or even suppressed if surfactants are ionically crosslinked such that their mobility at the liquid-liquid interface is reduced. To test our expectation, we produce water-oil-water double emulsions containing fluorescein in their cores. Indeed, the vast majority of fluorescein contained in double emulsions stabilized with ionically crosslinked FSHPEG900HA is retained for more than 14 days, which is the duration of our experiment, as shown in the micrograph in **Figure 4c** and by the blue triangles in **Figure 4d**. By contrast, in the absence of Fe^{3+} crosslinkers, fluorescein is very rapidly released from FSHPEG900HA stabilized double emulsions, as shown by the orange triangles in Figure 4d. Even faster fluorescein release is observed if double emulsions are stabilized with 2 mM FSH_2-Jeffamine600, a non-functionalized surfactant, as shown by the red circles in Figure 4d. These results demonstrate that our catechol-functionalized surfactants constitute an elegant way to overcome cross-contaminations that typically occur between surfactant-stabilized emulsions. Hence, these surfactants have the potential to significantly increase the usefulness of drops as picoliter-sized tight vessels for conducting high-throughput screening assays with an unprecedented accuracy.

Catechol-functionalized materials have a high affinity towards iron-presenting surfaces.[49] We therefore expect capsules presenting Fe^{3+} complexed catechols at their surfaces to have a high affinity to each other if not all catechols are complexed to Fe^{3+} ions. To test this expectation, we produce monodisperse aqueous drops (pH = 8) with a diameter of 114 μm that are dispersed in HFE-7100 containing 2 mM of the catechol-functionalized FSHPEG900HA surfactant and 0.6 mM Fe^{3+}. Monodisperse drops are deposited onto a layer of an aqueous solution (pH = 8) where they self-assemble into a densely packed monolayer, as shown in the optical micrograph in **Figure 5a**. Drops adhere to each other to form an integral monolayer, as indicated by the collective movement of the layer. If adjacent capsules are linked through ionic bonds, the films should be self-healing. Indeed, when the ruptured interfaces are brought in contact, they self-heal, as shown in the time lapse optical micrographs in Figure 5a and **Movie S5**. These results indicate that a significant fraction of free catechols are present at the drop surface.

The good mechanical stability, high deformability, and stickiness of our capsules open up a new field of their application: If up-concentrated, they have the potential to serve as inks that can be 3D printed. To test if these capsules indeed can be processed into granular macroscopic materials using 3D printing, we assemble aqueous drops dispersed in HFE-7100 containing 2 mM of the catechol-functionalized FSHPEG900HA surfactant and 0.6 mM Fe^{3+}. We up-concentrate the drops and eject them through a pipette tip at a controlled flow rate to form a 3D hydrogel, as shown in the time-lapse photographs in **Figure 5b** and **Movie S6**. Remarkably, the ejected solution is sufficiently viscoelastic to ensure good control over the shape of the processed macroscopic materials, as shown in Figure 5b. Indeed, even free-standing structures such as bridges can be 3D printed, as shown in **Figure 5c**. The printed materials are made of individual compartments with well-defined sizes that are linked to their neighbours, resulting in granular structures, as shown in **Figure 5d**. These results show feasibility to not only use these capsules as dispersed delivery vehicles but also as building

blocks of macroscopic materials with well-defined structures and locally varying compositions. However, these structures are viscoelastic such that they change their shape over time. To test if we can use the same capsules to produce mechanically stable, elastic granular hydrogels, we eject the concentrated solution into an aqueous solution whose pH is adjusted to 12 to induce covalent crosslinking of catechols,[50] as shown in **Figures 6d and e** and **Movie S7**. Indeed, if printed under these conditions, the formed threads are much more stable, as indicated in the time-lapse photographs in **Figure 5e**, yet the regular, granular structure is preserved, as shown in **Figure 5g**. These results suggest that the capsule shells are covalently cross-linked. As a result of the covalent cross-links, adjacent layers do not stick to each other anymore, as shown in **Movie S8**. These results open up a new field of use of capsules with thin shells, namely their collective assembly to additive manufacture macroscopic granular materials with well-defined structures and compositions that vary over short length scales.

2. Conclusion

We introduce new viscoelastic, sticky capsules that are deformable and mechanically sufficiently robust to be additive manufactured into macroscopic materials. Capsules are composed of catechol-functionalized block copolymer based surfactants that are ionically crosslinked at the drop surface to form viscoelastic shells. The resulting mechanically stable capsules are for practical purposes impermeable even towards low molecular weight encapsulants, thereby enabling their use as truly closed yet dynamic containers that do not suffer from cross-contaminations. Importantly, the mechanical stability and viscoelastic behaviour of these capsules open up a new field of their use in additive manufacturing: They can be 3D printed into proto-tissue-like cm-sized materials with well-defined structures. This feature offers new possibilities for additive manufacturing of functional soft materials with

structures that are well-defined over many different length scales and locally varying compositions.

3. Experimental Section

Surfactant Synthesis:

Chemicals: All chemicals, namely fluorinated oils HFE-7100 and HFE-7500 (3M, USA), the fluorinated block of the surfactant FSH (Krytox 157 FSH, Chemours, USA), polypropylene glycol (PPG 2000 g/mol, Acros Organics), thionyl chloride and chloroform (Merck, Germany), dichloromethane (DCM), anhydrous Ethyl acetate (EtAc), methanol (MeOH), triethylamine, dopamine hydrochloride (Dopa), N,N-dicyclohexylcarbodiimid (DCC) (Sigma-Aldrich), anhydrous N,N-Dimethylformamide (DMF) and 3-(3,4,-Dihydroxyphenyl)propionic acid (hydrocaffeic acid, HA) (Abcr, Germany), and N-Hydroxysuccinimide (NHS) and stearoyl Chloride (TCI, Japan) were used as received.

FSHDopa synthesis:

All the reactions are performed under argon atmosphere using dry glassware. 1 mol equivalent of FSH is dissolved at 0.2 gmL^{-1} in HFE-7100, dried with molecular sieves, and the solution is degassed with argon. 10 mol equivalents of thionyl chloride is added to the solution under argon atmosphere to activate the carboxylic end group of the FSH. This reaction is refluxed at 65°C for 2 hours. Under reduced pressure and at 90°C the excess thionyl chloride is removed, resulting in the pure activated FSH. The FSH is subsequently re-dissolved in HFE-7100. 2.5 mol equivalents of dopamine is dissolved in DMF and the solution degassed with argon before it is mixed with activated FSH. 2.5 mol equivalents of triethylamine is added to the reaction to drive the reaction to completion. The reaction is refluxed overnight at 65°C. The solution is filtered through a filter paper, and all the solvents are removed under reduced pressure. The product is purified using a mixture of water and

HFE-7100 and subsequently washed using a mixture of HFE-7100 and methanol. The precipitates are removed through centrifugation at 3000 g for 15 min (Mega Star, 1.6R, VWR). This washing step is repeated three times before the product is dried using a rotary evaporator (Hei-VAP, Heidolph, Germany) and freeze dryer (FreeZone 2.5, Labconco, USA).

FSHPEG900HA synthesis:

1 mol equivalent of hydrocaffeic acid is dissolved in dry ethyl acetate at 0.04 gmL^{-1}, and 1 mol equivalent NHS is added to the reaction. 1 mol equivalent of DCC is dissolved in ethyl acetate and added to the NHS HA mixture that is stirred overnight under inert atmosphere. The product HA-NHS is filtered through a filter paper and dried under reduced pressure. 1 mol equivalent of HA-NHS is dissolved at 0.11 gmL^{-1} in dry ethyl acetate and bubbled with argon. 0.95 mol equivalent of the polyethylene glycol Jeffamine ED-900 (Huntsman, USA) is dissolved in dry ethyl acetate and added to the HA-NHS solution and stirred overnight. The solvent is removed using a rotary evaporator, resulting in the intermediate product H_2N-PEG-HA. FSH is activated as described for the synthesis of FSHDopa. 1.5 mol equivalent of H_2N-PEG-HA is dissolved in DCM and added to the activated FSH. 1 mol equivalent of triethylamine is added to drive the reaction to completion, and everything is refluxed overnight at 65°C. The solvent is removed, and the product is washed using a mixture of HFE-7100 and methanol, and they are centrifuged at 3000 g. This washing step is repeated three times. The final product is dried using a rotary evaporator and a freeze dryer.

SADopa synthesis:

1 mol equivalent of stearyl chloride is dissolved in anhydrous DMF under argon at 0.2 gmL^{-1}. 1.5 mol equivalents of dopamine is dissolved at 0.06 gmL^{-1} in DMF and cooled to 0°C. 3 mol equivalents of triethylamine is added to the dopamine and mixed with stearyl chloride. The mixture is heated to 65°C and stirred overnight under argon atmosphere. The reaction product

is extracted with water and ethyl acetate. This cleaning step is repeated three times before everything is dried in a rotary evaporator and a freeze dryer.

DiDopaPPG synthesis:

1 mol equivalent of propyleneglycol is dissolved in chloroform, and 10 mol equivalent of thionyl chloride is added. The solution is refluxed at 65°C for 2 hours. The excess thionyl chloride is removed under reduced pressure at 90°C. 4 mol equivalents of dopamine is dissolved in DMF, 1.5 mol equivalents of triethylamine is added, and the mixture is stirred overnight. The product is extracted with diethylether and water. Extraction is repeated three times before the solvents were removed using a rotary evaporator and freeze dryer.

Buckling test:

To test the buckling of the capsules we use a pendant drop setup (DSA-30 Krüss, Germany) to image the drops and to controllably retract the fluid contained in them.

Fabrication of microfluidic device:

We produce flow focussing microfluidic devices from poly(dimethylsiloxane) (PDMS) (Dow Corning, USA) using soft lithography. [1] The channel walls of single emulsion drop makers are rendered fluorophilic by injecting a HFE-7500-based solution containing 2 vol% of trichloro(1H,1H,2H,2H-perfluorooctyl)silane (Sigma-Aldrich, USA) for 10 min. To modify the surface of double emulsion drop makers, their channel walls are activated with 1M NaOH for 10 min before they are dried with compressed air. The first junction is rendered fluorophilic by treating this part of the channel with a HFE-7500-based solution containing 2 vol% of trichloro(1H,1H,2H,2H-perfluorooctyl)silane (Sigma-Aldrich, USA). The second junction, which is a 3D junction,[2] is rendered hydrophilic using an aqueous solution

containing 2 wt.% polydiallyldimethylammonium chloride (Sigma-Aldrich, USA). The solutions are left in the channels for 30 min before channels are dried with compressed air.

Production of emulsion drops:

Emulsion drops are produce using microfluidic flow focusing devices. Single emulsions are assembled by injecting the inner phase at flow rates varying between 2000 and 3000 µl/h using syringe pumps (Cronus Sigma 1000, Labhut, UK). The outer phase is injected at 4000 µl/h.

To produce double emulsions, an aqueous phase containing 6 wt.% PEG 6000 Da, 0.01 wt% Fluorescein Na salt, 0.3 M BICINE buffered at pH=8.5, and 0.02 mM Fe^{3+} is employed. The middle phase consists of HFE-7500 or HFE-7100 containing 2 mM of a surfactant. The outer phase is an aqueous solution containing 10 wt% partially hydrolysed polyvinyl alcohol (PVA) 13-18 kDa (Sigma-Aldrich, USA). Double emulsions are produced by injecting the inner phase at around 1000 µl/h, the middle phase at 1000-1300 µl/h and the outer phase at around 6000 µl/h. To avoid osmotic pressure gradients, that would result in a change in the dimensions of the double emulsions, the osmolarity of the inner and outer phase is matched using D(+)-saccharose (Carl Roth, Germany); the osmolarity of the solutions is quantified with an osmometer (Advanced Instruments, Fiske 210).

Quantification of the leakage:

To minimize the risk that the permeability of double emulsions is influenced by PVA present in the outer phase, double emulsions are washed three times using an osmotically balanced aqueous solution. 1 µl of washed double emulsions is added to 1.5 mL of an osmotically balanced aqueous solution, and emulsions are imaged every 10 min using a fluorescent microscope (Eclipse Ti-S, Nikon). The fluorescence images are analyzed using a custom-

made MATLAB code that quantifies the evolution of the fluorescent intensity of double emulsion cores over time.

3D printing of capsules:

2 mM FSHPEG900HA are dissolved in HFE-7100 containing Fe^{3+} ions at a 3:1 ratio. Iron is added to HFE-7100 from an ethanol-based solution containing 1M $FeCl_3$ (Sigma-Aldrich, USA). Single water in oil emulsions are produced using a PDMS microfluidic flow focusing device. An HFE-7100-based solution containing surfactants and Fe^{3+} is used as the continuous phase.

Supporting Information
Supporting Information is available from the Wiley Online Library or from the author.

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Competing Interests:
A European Patent Application No 18170186 has been filed on catechol-functionalized surfactants.

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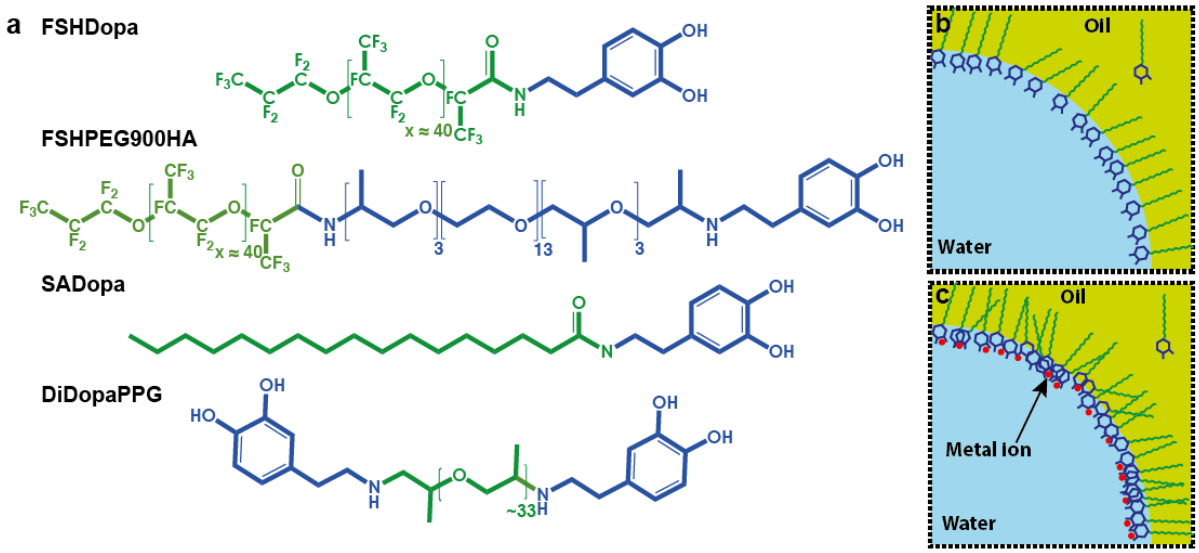

Figure 1. Catechol-functionalized surfactants. (a) Chemical structures of different catechol-functionalized surfactants. (b,c) Schematic illustrations of emulsion drops stabilized with catechol-functionalized surfactants in the (b) absence and (c) presence of Fe^{3+} ions that cross-link the surfactants at the interface.

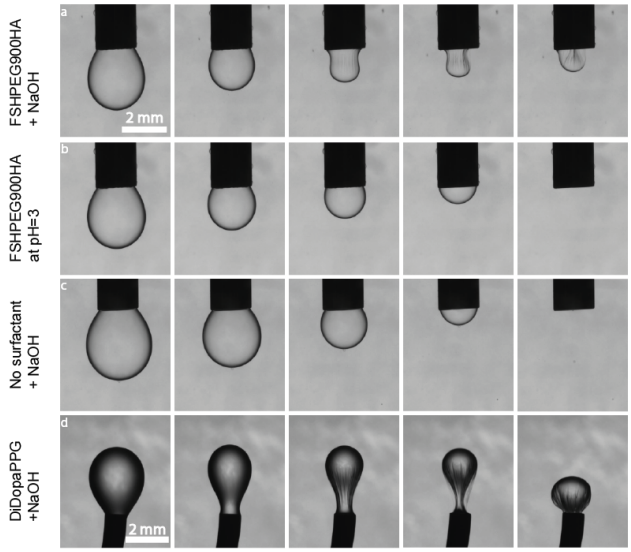

Figure 2. Time-lapse optical micrographs of oil drops containing catechol surfactants that are dispersed in aqueous solutions containing 1 mM $FeCl_3$ acquired during the retraction of the oil phase. (a, b) Drops composed of HFE-7500 containing 2 mM FSHPEG900HA (a) with and (b) without 0.01 M NaOH in the continuous phase. (c) Control experiments of HFE-7500-based drops containing no surfactant. Drops are formed inside an aqueous solution containing 1 mM $FeCl_3$. (d) Drop composed of toluene, containing 2 mM DiDopaPPG dispersed in an aqueous solution containing 1mM $FeCl_3$ and 0.01 M NaOH.

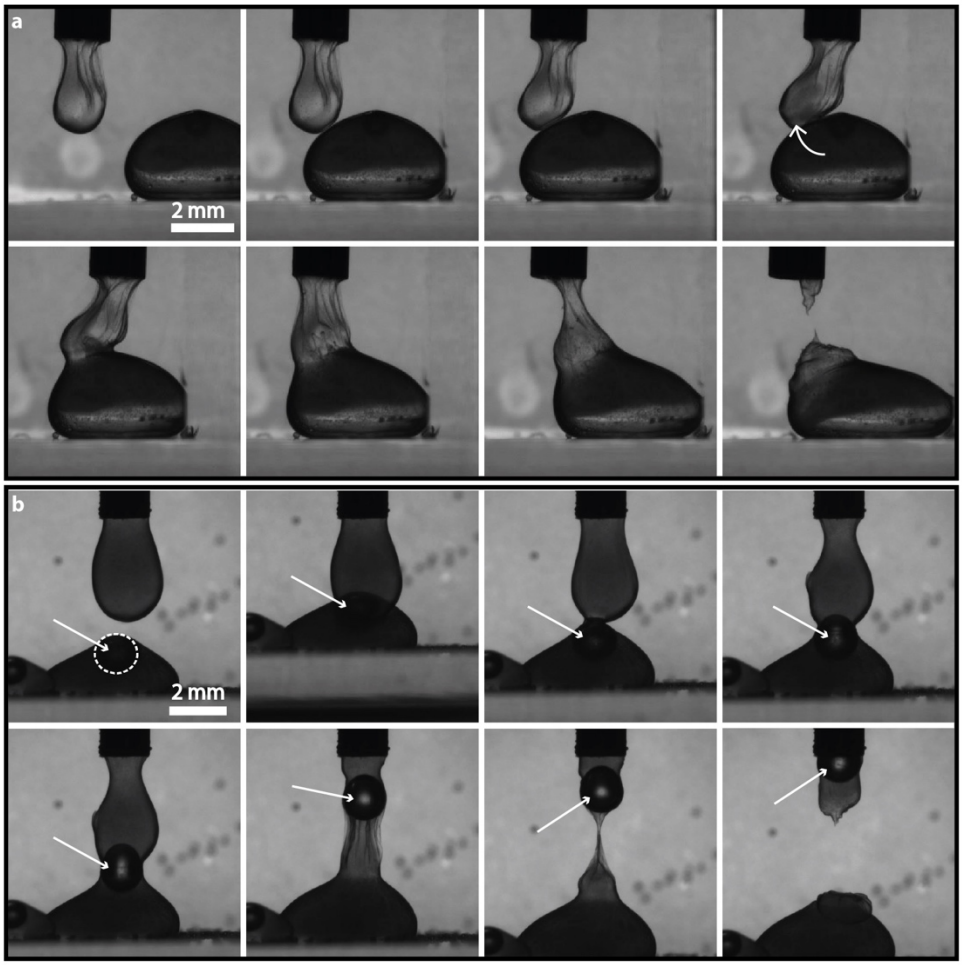

Figure 3. Time-lapse photographs of fluorinated drops stabilized with ionically crosslinked catechol-functionalized surfactants. Drops composed of HFE-7100 are loaded with 6 mM Fe^{3+} and 2 mM FSHDOPA and surrounded by a buffered aqueous solution. Catechol-functionalized surfactants are crosslinked with Fe^{3+} to form viscoelastic shells that (a) can be merged if two drops come in contact and (b) allow exchanging even large reagents, as exemplified by a 1.5 mm diameter air bubble that is initially trapped in the sessile drop and transferred to the pendant drop, as indicated by the white arrows.

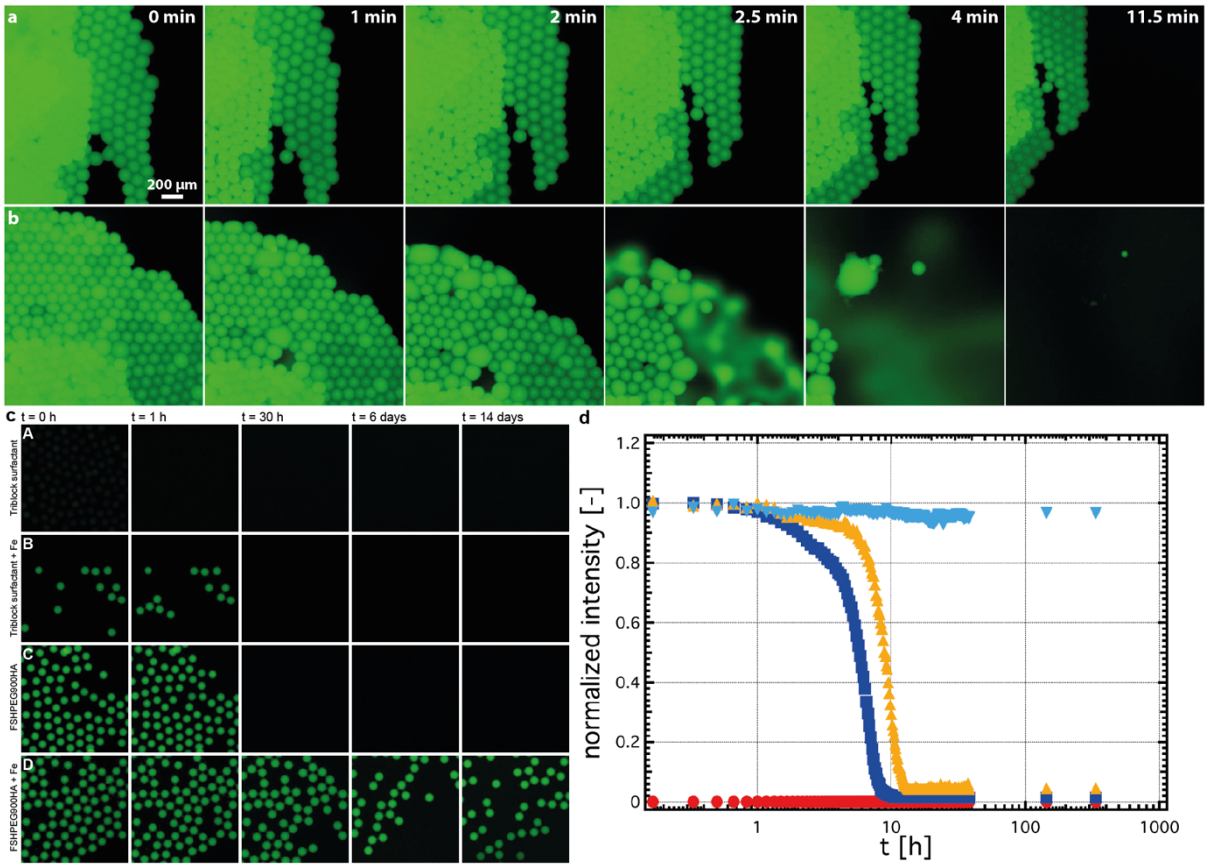

Figure 4. (a,b) Fluorescence microscopy images of fluorescently labelled single emulsion drops floating on a buffered Fe^{3+}-containing water solution (pH=8.5). Drops are stabilized with (a) catechol-functionalized FSHPEG900HA and (b) unfunctionalized FSH-Jeffamine2000. Drops stabilized with unfunctionalized surfactants rupture during the evaporation of the oil whereas those stabilized with catechol-functionalized surfactants remain intact. (c,d) Permeability of double emulsions. (c) Fluorescent micrographs of double emulsions containing fluorescein acquired after they have been stored at room temperature for 0 h, 1 h, 30 h, 6 days, and 14 days. Double emulsions are stabilized with (A, B) 2 mM unfunctionalized FSH_2-Jeffamine600 and (C, D) the catechol functionalized FSHPEG900HA. The core of the double emulsions contains (A,C) water and fluorescein, (B,D) Fe^{3+}, fluorescein, and BICINE to buffer the pH at 8.5. (d) Normalized fluorescent intensity of the double emulsions cores as a function of the incubation time at room temperature. All double emulsions are dispersed in water where the osmotic pressure is balanced. Double emulsions

whose core has a neutral pH and contains no iron stabilized with FSH_2-Jeffamine600 (●), contains BICINE and iron stabilized with FSH_2-Jeffamine600 (▲), has a neutral pH and contains no iron stabilized with FSHPEG900HA (■) and contains BICINE and iron and stabilized with FSHPEG900HA (▼).

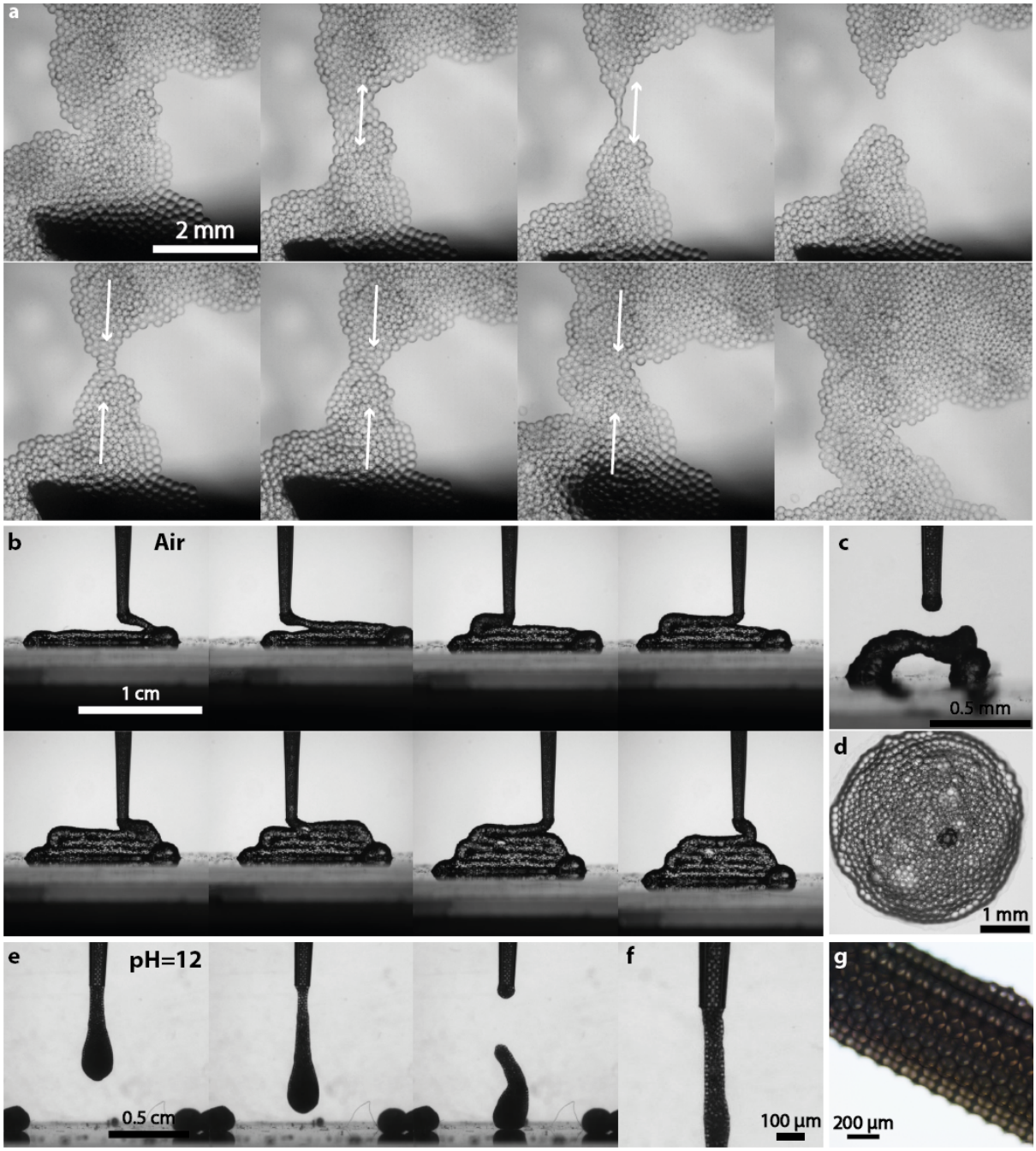

Figure 5. (a) Time-lapse optical micrographs of self-healing films composed of viscoelastic capsules. Aqueous drops (pH=8) dispersed in HFE-7100 containing FSHPEG900HA and Fe^{3+} are deposited onto an aqueous solution (pH=8). When the oil evaporates, a film composed of individual capsules form. These plastically deformable films self-heal when broken parts are brought in contact. Arrows indicate the direction of force applied on the film. 3D printing of viscoelastic capsules in (b-d) air and in (e-g) aqueous solutions. (b) Time-lapse photographs of capsules whose core is composed of an aqueous solution (pH=8.5). Capsules are made

from water in HFE-7100 emulsion drops stabilized by 2 mM FSHPEG900HA and Fe^{3+}. (c) Photograph of a 3D printed suspended bridge composed of additive manufactured viscoelastic capsules. (d) Cross-section of a 3D printed structure revealing its granular structure. (e) Time-lapse photographs of densely packed capsules that are printed into an aqueous solution whose pH is 12. (f) Zoom-in on the ink composed of up-concentrated capsules as it is ejected. (g) Microscope image of the resulting printed structure composed of covalently crosslinked capsules.

Keyword Keywords: (capsules, catechols, surfactants, 3D printing)

*Gianluca Etienne, Esther Amstad**

Bio-Inspired Self-Healing Capsules: Delivery Vehicles and Beyond

Supporting Information

Bio-Inspired Self-Healing Capsules: Delivery Vehicles and Beyond

*Gianluca Etienne, Esther Amstad**

G. Etienne, Prof. E. Amstad
Soft Materials Laboratory, Institute of Materials, École Polytechnique Fédérale de Lausanne (EPFL), CH-1015 Lausanne, Switzerland
E-mail: esther.amstad@epfl.ch

Buckling of drops:

To test if catechol-functionalized surfactants that do not contain any hydrophilic spacing block also form viscoelastic shells at the drop surface in the presence of Fe^{3+} ions, we form an HFE-7500 drop containing 2 mM FSHDopa in an aqueous solution containing 1 mM Fe^{3+} and NaOH. When the HFE-7500 is slowly retracted, the drop surface starts to buckle, indicating that a shell formed, as shown in the time lapse photographs in Figure S1a. Compared to an unfunctionalized surfactant FSH_2-Jeffamine900, we do not observe any buckling immediately after drop formation, as shown in Figure S1b. Note that if the amount of base added is increased, thin, rather fragile shells become apparent, even for drops that do not encompass any surfactants or those that contain catechol-free surfactants. This shell formation most likely is caused by Fe^{3+} ions that aggregate under these basic conditions, and the resulting particles accumulate at the surface, thereby forming Pickering emulsions.

To test if the formation of viscoelastic shells is limited to fluorinated surfactants, we form drops composed of ethyl acetate, 2 mM SADopa, and 0.6 mM Fe^{3+} in a basic aqueous solution (pH=9). Indeed, also in this case, we observe the formation of a shell at the drop surface, as

shown in Figure S1c. These results suggest that the formation of these shells is not limited to fluorinated surfactants but occurs for any catechol-modified surfactant.

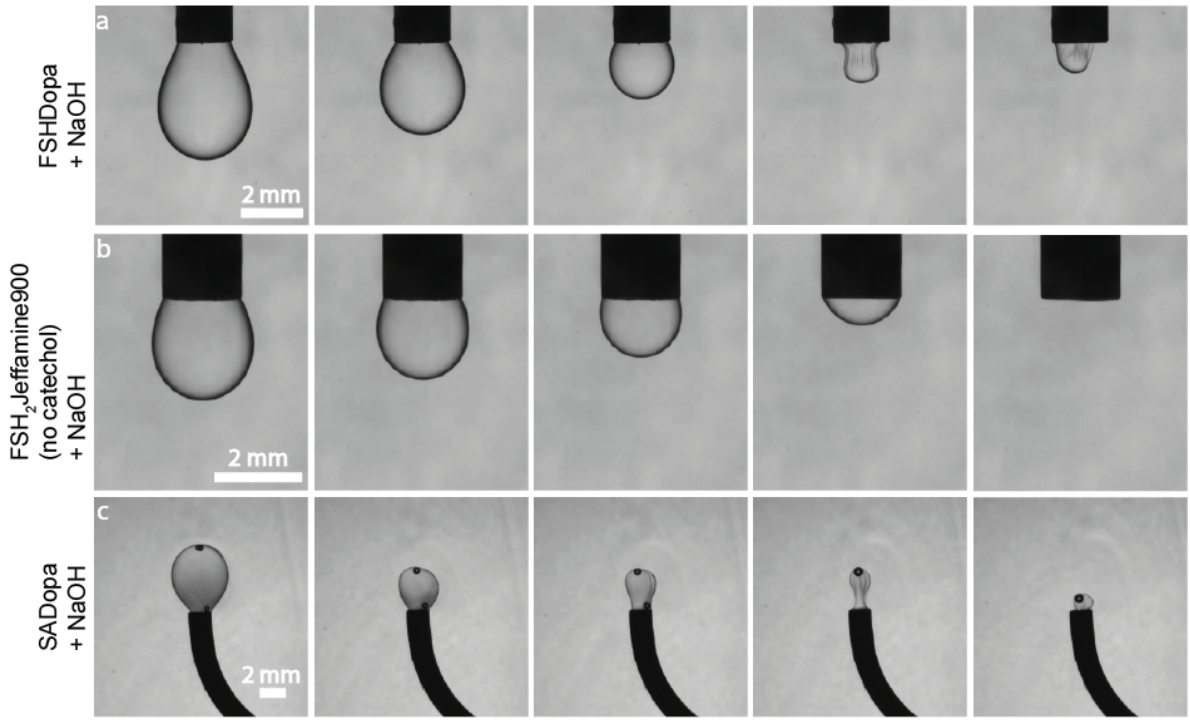

Figure S1. Time lapse photographs of a HFE7500-based drop containing (a) 2 mM FSHDopa (b) 2 mM of an unfunctionalized surfactant, FSH_2-Jeffamine900, and (c) an ethyl acetate-based drop containing 2 mM SADopa and Fe^{3+} formed in a basic aqueous solution (pH=9).

Characterization of catechol-Fe^{3+} interactions:

To test if catechol-functionalized surfactants form complexes with Fe^{3+} ions, we acquire UV/VIS spectra. Because SADopa is poorly soluble in water, we dissolve it in ethanol at 4 mM. The resulting absorption spectra display a peak at 280 nm, as shown in Figure S2. We assign this peak to the absorption of catechols.[3] If Fe^{3+} ions are added to the solution, the absorption peak is shifted to 250 nm, indicating that Fe^{3+} ions interact with catechols. The observed shift is much smaller than that measured for catechol/Fe^{3+} complexes formed in aqueous solutions.[4] We assign this difference to the different solvent we use.

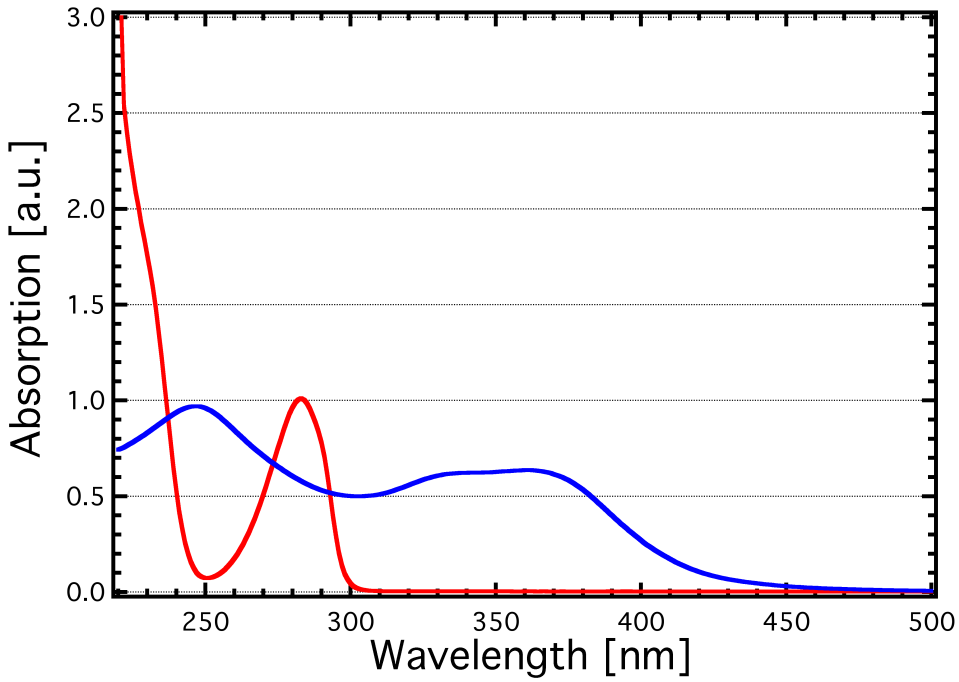

Figure S2. UV/VIS spectra of the catechol-functionalized surfactant SADOPA. UV/VIS traces of SADopa dissolved in ethanol with (___) and without (___) Fe^{3+}.

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