Influence of the hydrophile–lipophile balance of perfluorinated surfactants on the emulsion stability

Gaia De Angelis and Esther Amstad*

Received: 1 December 2023 / Accepted: 9 March 2024 / Published online: 18 April 2024

Impact statement
This paper describes the influence of the HLB value of perfluorinated block-copolymer-based surfactants on the stability of water-in-perfluorinated oil drops. It demonstrates that water-in-perfluorinated oil drops are most stable if the HLB value of the surfactants is around 2.5.

Emulsions are omnipresent in our everyday life; for example, in food, certain drug and cosmetic formulations, agriculture, and as paints. Moreover, they are frequently used to perform high-throughput screening assays with minimum sample volumes. Key to the successful use of emulsions is a good drop stability. Most frequently, drops are stabilized with surfactants composed of hydrophilic and hydrophobic parts. Appropriate surfactants are often selected based on the ratio of their hydrophilic to the hydrophobic parts, their hydrophilic–lipophilic balance (HLB), which determines their solubility. However, how the HLB value of perfluorinated surfactants influences the emulsion stability remains to be determined. To address this question, we report a benign and cost-effective synthesis of diblock-copolymer surfactants that consist of a perfluorinated block covalently linked to a hydrophilic poly(ethylene glycol) (PEG)-encompassing block. The compositions of the fluorophilic and hydrophilic blocks are very similar to those of commercially available triblock-copolymer surfactants commonly used within the microfluidic community that employs poly(dimethylsiloxane) (PDMS)-based devices. By deliberately tuning the ratio of the hydrophobic to the hydrophilic blocks of our diblock-copolymer surfactants, we obtain HLB values varying between 0.9 and 3.3. We demonstrate that the best emulsion stability is obtained if the molecular weight ratio of the hydrophobic to the hydrophilic blocks is between 5 and 7, corresponding to HLB values between 2.5 and 3.3. Importantly, our cost-effective surfactant displays a similar performance to that of the rather costly commercially available Pico-Surf surfactant. Thereby, this study presents guidelines for a cheap, benign, and targeted synthesis of appropriate perfluorinated surfactants that efficiently stabilize water-in-perfluorinated oil emulsions.

Introduction

Emulsions are drops dispersed in a second immiscible liquid. Many emulsions are thermodynamically unstable because they possess a much higher interfacial area than a phase-separated system composed of the same types and volume ratios of fluids. As a result, most of these emulsions tend to coalesce.[1] The coalescence can be delayed if drops are stabilized with ionic and nonionic low-molecular-weight surfactants,[2,3] nanoparticles,[4] proteins,[5] and appropriate polymer-based surfactants.[6]

The emulsion stability depends on the choice of the oil and aqueous phase, the composition and concentration of surfactants present in the continuous phase, which also influences their adsorption kinetics, the surrounding conditions such as temperature, pH, and the composition and concentration of solutes present in either of the phases.[7]

Gaia De Angelis, Soft Materials Laboratory, Institute of Materials, École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland; National Center of Competence in Research (NCCR) Bio-Inspired Materials, Fribourg, Switzerland;
Esther Amstad, Soft Materials Laboratory, Institute of Materials, École Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland; National Center of Competence in Research (NCCR) Bio-Inspired Materials, Fribourg, Switzerland; esther.amstad@epfl.ch
*Corresponding author
doi:10.1557/s43577-024-00704-x

Unfortunately, the selection of appropriate surfactants is in many cases rather empirical, often rendering the formulation of new emulsions time- and resource-consuming.

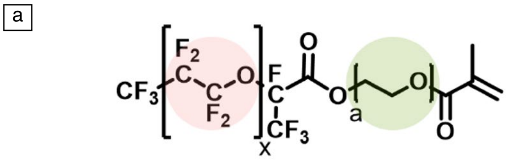
Drops possessing well-defined sizes are frequently fabricated with poly(dimethylsiloxane) (PDMS)-based microfluidic devices.[8] These aqueous drops are typically dispersed in a perfluorinated oil for its compatibility with PDMS.[9] Such drops are most frequently stabilized with block-copolymer surfactants composed of a hydrophilic, PEG-containing block that is covalently linked to one or two fluorinated blocks.[10–12] These drops are used to analyze or handle minimum amounts of reagent volumes, for example for DNA analysis,[13] cell sorting,[14,15] drug discovery,[16,17] cell fusion,[18] diagnostics,[19] biological assays,[20] and chemical synthesis.[21] To address the diverse needs of these applications in terms of drop stability and compatibility with a wide range of encapsulants, perfluorinated surfactants possessing different functionalities, including perfluoroalkyl carboxylates,[22] perfluoroalkyl sulfonates,[23] and perfluoropolyethers,[24–26] with hydrophobic-to-hydrophilic block ratios ranging from 3 to 40, corresponding to HLB values ranging from 0.5 to 4.2 have been introduced. The most commonly used surfactants have been commercialized, thereby making this surfactant accessible to a larger community, albeit at rather high costs. Unfortunately, guidelines on the selection of the most appropriate fluorinated surfactant are still missing such that in many cases, different types of surfactants must be tested before emulsions displaying an appropriate stability are obtained. This empirical surfactant selection is rather costly and time-consuming.

Here, we introduce a cost- and energy-efficient synthesis of perfluorinated diblock surfactants. We systematically study the influence of the HLB value of perfluorinated diblock surfactants on their packing density and the interfacial tension and relate these parameters to the emulsion stability. These studies reveal an optimum HLB value for these perfluorinated diblock-copolymer surfactants of 2.5, independent of surfactant concentration.

Results and discussion

To stabilize water-in-oil emulsions, we synthesize oil-soluble block-copolymer surfactants and deliberately vary the molecular weight ratio of their hydrophobic to hydrophilic blocks. To ensure the surfactant is soluble in the oil, we chose block ratios leading to HLB values below 10. We use a model surfactant consisting of a perfluorinated block, Krytox, that we covalently link to a hydrophilic, poly(ethylene glycol) mono methacrylate (PEGMMA) block through an esterification reaction, as schematically shown in **Figure 1**a and detailed in Supplementary information (SI) Figure S1. We activate the carboxylic acid at the end of the perfluorinated block using oxalyl chloride, chosen for its milder reactivity compared to the commonly utilized thionyl chloride. This activation takes place at room temperature, obviating the need for reflux or solvents. Any residual oxalyl chloride is removed using a rotary evaporator, eliminating the requirement for energy-consuming high-temperature synthesis or cryogenic baths. The activated Krytox FSH is reacted with PEGMMA, dissolved in dichloromethane (DCM), and refluxed at 65°C. The resulting surfactant is purified through a series of centrifuge washes before it is freeze-dried. We confirm the successful coupling of the surfactants through Fourier transform infrared (FTIR) and nuclear magnetic resonance (NMR) spectroscopy, as shown in SI Figure S2a–d and S3, respectively. To avoid covalent cross-linking of the perfluorinated block on both sides of the hydrophilic block, which would lead to the formation of triblock surfactants, we choose a mono methacrylated PEG. We employ hydrophobic, commercially available Krytox blocks with molecular weights of 2500 g/mol and 7500 g/mol and hydrophilic commercially available PEGMMA blocks with molecular weights of 360 g/mol and 500 g/mol. By coupling the different commercially available hydrophobic and hydrophilic blocks in the four possible combinations, we obtain surfactants with molecular weight ratios of their hydrophobic to the hydrophilic blocks ranging from 5 to 21, corresponding to HLB values between 0.9 and 3.3, as illustrated in Figure 1b.

Our process offers a remarkable cost advantage. We can produce these surfactants at up to tenfold lower costs compared to those associated with the purchase of commercially available alternatives, such as Pico-Surf and FluoSurf. Note that the blocks our surfactant is built from are very similar or identical to those used to synthesize commercially available perfluorinated surfactants. However, most commercially available fluorinated surfactants are primarily composed of triblock copolymers, in stark contrast to our surfactant that is a diblock copolymer.



b

Surfactant	Mw of hydrophobic block (Da)	Mw of hydrophilic block (Da)	Ratio hydrophobic to hydrophilic	HLB value
FSL-PEGMMA500	2500	500	5	3.3
FSL-PEGMMA360	2500	360	7	2.5
FSH-PEGMMA500	7500	500	15	1.3
FSH-PEGMMA360	7500	360	21	0.9

Figure 1. (a) Molecular structure of the diblock-copolymer surfactants composed of a hydrophobic Krytox block and a hydrophilic PEGMMA block with (b) the molecular weights (MW) of the different blocks, the molecular weight ratio of the hydrophobic to hydrophilic blocks, and their corresponding hydrophilic–lipophilic balance (HLB) values.

All the reported surfactants are soluble in perfluorinated oils, such as HFE7100. Yet, we expect the ratio of the hydrophobic to hydrophilic blocks of these surfactants to influence the interfacial tension between water and HFE7100. To test this expectation, we quantify the interfacial tension between water and the surfactant-containing oil through interfacial tension measurements. We fix the surfactant concentration at 1 wt%, corresponding to molar concentrations ranging from 2 to 4 mM. These values exceed the critical micelle concentrations of all the tested surfactants, as shown in SI Figure S4. Indeed, the interfacial tension decreases with increasing ratio of the hydrophobic to the hydrophilic blocks until the HLB value reaches 2.5, whereafter the interfacial tension slightly rises again, as shown in **Figure 2**a. This minimum interfacial tension value is obtained for the surfactant with a HLB value of 2.5. It is very similar to that achieved with the commercially available surfactant Pico-Surf that exhibits an interfacial tension of 5 mN/m. Yet, we cannot accurately determine the HLB value of the commercial surfactant as its exact composition and purity is unknown.

According to the Bancroft's rule, emulsions are more stable if the surfactant is dissolved in the continuous phase, which in our case is the oil.[27] A HLB value of at most 3.3 assures a good solubility of the surfactant in the oil. We expect the hydrophilic block to be sufficiently long to ensure some anchoring of the surfactant at the liquid–liquid interface yet, to be sufficiently small to allow a dense packing at this interface. To test this expectation, we quantify the surfactant packing density at the water–air interface using Langmuir trough isotherms and plot this parameter as a function of their HLB values. Remarkably, the packing densities of all the tested surfactants are similar, 0.14 ± 0.02 nm^{-1}, as shown in Figure 2b. We assign this result to the hydrophilic blocks whose radii of gyration vary between 0.30 nm and 0.33 nm, such that their volumes, which limit the surfactant packing density in our Langmuir trough setup, are rather similar.

To compare the packing density of our surfactants to that of commercially available counterparts, we quantify the packing density of the commercially available surfactant Pico-Surf. Remarkably, Pico-Surf exhibits a packing density of 0.33 ± 0.02 nm^{-2}, which is twofold higher than what we observe for our fluorinated surfactants. Yet, a direct comparison of the two types of surfactants is challenging due to the lack of information regarding the composition and purity of the Pico-Surf surfactant. Nevertheless, the significant difference in packing density suggests that Pico-Surf contains a large fraction of triblock copolymers.

Emulsion stability is closely tied to interfacial tension, which, in turn, is linked to the molecular composition of surfactants. To assess how the HLB values of our perfluorinated diblock-copolymer surfactants influence the stability of water-in-oil drops, we form monodisperse single emulsion drops using a microfluidic flow focusing device. The drops display an average diameter of 100 μm and a standard deviation of 18 μm, independent of the diblock-copolymer surfactant used to stabilize them. To prevent liquid evaporation, which would affect the stability of the emulsions, we immerse them in an excess of HFE7100 and tightly cover the samples with an adhesive film. As expected, emulsion drops that are not stabilized with any surfactant coalesce within seconds, as shown in SI Figure S5. Drops stabilized with surfactants that lower the interfacial tension to around 20 mN/m are only stable for up

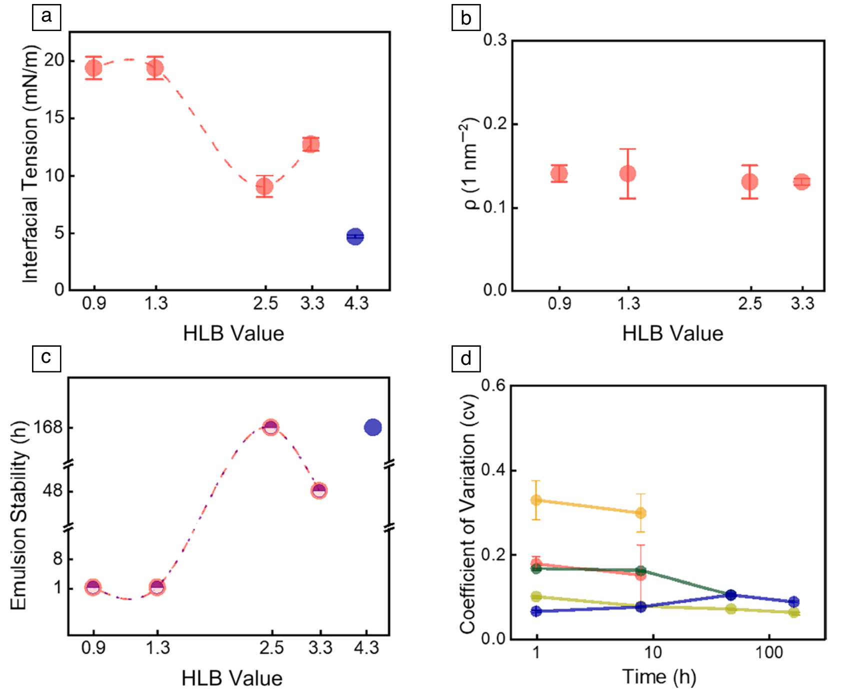


Figure 2. (a) Interfacial tension between water and HFE7100 containing 1 wt% surfactant, and (b) packing density of surfactants at the water–air interface. (c) Stability of water-in-oil drops produced with microfluidic devices stabilized with 1 wt% (orange-filled circle) and 5 mM (magenta half-filled circle) of different surfactants as a function of their hydrophilic–lipophilic balance (HLB) values. (d) Coefficient of variation measured from 1 h to seven days for emulsion drops stabilized with surfactants with HLB values of 0.9 (orange-filled circle), 1.3 (yellow-filled circle), 2.5 (gray-filled circle), and 3.3 (green-filled circle). Emulsions stabilized with surfactants with HLB values of 1.3 and 3.3 phase separate after 48 h and seven days, respectively. Blue-filled circles correspond to the coefficient of variation of water-in-mineral oil emulsions that have been stabilized with a commercially available hydrocarbon-based surfactant, Span80. Each experiment was repeated three times.

to 1 h, as indicated by the rapidly increasing coefficient of variation in Figure 2d. By contrast, emulsion drops with interfacial tensions of 13 and 9 mN/m are stable for two and seven days, respectively, as shown in Figure 2c. As a consequence of the good emulsion stability, their coefficients of variation remain within experimental error unchanged over at least seven days, as shown in Figure 2d. Importantly, the emulsion stability does not significantly change if we increase the surfactant concentrations to 5 mM, as shown in SI Figure S6. These results suggest that the emulsion stability is primarily determined by the composition of the surfactants and not by their concentration, as long as the surfactant concentration exceeds its CMC.

To test if the emulsion stability depends on the oil composition, we exchange HFE7100 with HFE7500. HFE7100 is a mixture of linear methoxyperfluorobutane and branched methyl nonafluoroisobutyl ether. By contrast, HFE7500 is mainly composed of a branched compound, 2-(trifluoromethyl)-3-ethoxydodecafluorohexane, such that it has a much higher boiling point. Despite the different chemical composition of the oil, emulsions stabilized with the FSL-PEGMMA360 surfactant remain intact for up to seven days, as shown in SI Figure S7. This result indicates that the oil composition does not significantly affect the emulsion stability, as long as the surfactant possesses a high solubility in it.

To compare the stability of emulsions produced with our best surfactant to those produced with the commercially available Pico-Surf surfactant, we produced water-in-oil emulsions from an oil-containing 1 wt% Pico-Surf surfactant. We monitor the emulsion stability over seven days using optical microscopy. The stability of the emulsions achieved with our best surfactant is very similar to that of emulsions produced with the Pico-Surf surfactant, as shown in SI Figure S8.

Most industrially relevant emulsions encompass hydrocarbon oils. These emulsions must be stabilized with surfactants containing hydrocarbon-based surfactants. Hydrocarbon-based blocks have much lower molecular weights compared to fluorinated counterparts displaying similar dimensions. Hence, we do not expect the optimum HLB value determined for perfluorinated diblock copolymers to correspond to that valid for hydrocarbon-based counterparts. To test this expectation, we assess the stability of water-in-mineral oil emulsions that are stabilized with Span80, which has a HLB value of 4.3. We dissolve Span80 in mineral oil at a concentration of 2 wt%, a concentration commonly used in the literature.[28] These emulsions are stable for up to seven days, as shown in SI Figure S9. This comparison shows that our best fluorinated surfactant achieves emulsion stabilities, which are similar to those of hydrocarbon-based emulsions stabilized with a commercial hydrocarbon-based surfactant, Span80, showcasing its effectiveness and versatility.

Conclusions

We synthesize four surfactants with varying molecular weight ratios of perfluorinated to hydrophilic blocks, ranging from 5 to 21, such that their HLB values vary between 0.9 and 3.3. To achieve this goal, we introduce a cost-effective, scalable, benign synthesis of diblock-copolymer surfactants composed of a perfluorinated block that is covalently linked to a PEG-containing block. We demonstrate that perfluorinated diblock surfactants with HLB values between 2.5 and 3.3 lower the interfacial tension between perfluorinated oils and water most efficiently, leading to the best emulsion stability. Indeed, the interfacial tension as well as the emulsion stability reached with the best surfactant we tested are very similar to those obtained for emulsions stabilized with the commercially available Pico-Surf surfactant. Yet, our surfactant is approximately tenfold cheaper than the commercially available counterpart and can be synthesized in batches as large as 10 g. These findings offer crucial insights for the targeted, cost-effective synthesis of optimized surfactants that efficiently stabilize water-in-perfluorinated oil emulsions.

Materials and methods

All chemicals, namely anhydrous *N*,*N*-dimethylformamide (DMF), dichloromethane (DCM), methanol (MeOH), poly(ethylene glycol) methacrylate (MW 360 and 500 g/mol), hexafluorobenzene, Span 80, and mineral oil (Sigma-Aldrich), fluorinated blocks of the surfactants FSH and FSL (Krytox 157 FSH and Krytox 157 FSL, Chemours, USA), Pico-Surf (Sphere Fluidics), and fluorinated oil HFE7100 (3M, USA), are used as received.

FSX-PEGMMAX synthesis

Krytox FSX (5 g) is added to a round-bottom flask and sealed using a septum. The catalyst, *N*,*N*-dimethylformamide (1 drop) is added dropwise. Two mol equivalents of oxalyl chloride are carefully added to the flasks drop by drop using a syringe that has been purged with argon beforehand. The resulting mixture is stirred at room temperature for 4 h, yielding a faint yellow, somewhat opaque product. Excess oxalyl chloride is removed by reducing the pressure to 1 mbar (Hei-VAP, Heidolph, Germany), at 50℃ for 2 h. Subsequently, the activated FSX is dissolved in 10 mL of HFE7100, leading to a clear, pale-yellow solution.

To couple PEGMMAX to Krytox, 1.1 mol equivalents of PEGMMAX are dissolved in 5 mL of dry dichloromethane. This PEG solution is combined with the activated Krytox and left to reflux overnight at 65℃ in an argon atmosphere. This process results in a cloudy, white product. To purify this product, it is dissolved in 2 mL of HFE7100, before 50 mL of methanol is added. This solution is centrifuged at 3000 rpm and 3℃ for 15 min (Mega Star, 1.6R, VWR) to precipitate the product. The liquid supernatant is removed, and this washing procedure is repeated twice. The precipitated product is vacuum-dried at a pressure of 1 mbar and a temperature of 40℃ for 30 min. The product is freeze-dried overnight (FreeZone 2.5, Labconco, USA). The final product has a white, cloudy appearance. FTIR spectra of the products can be found in SI Figure S2a–d. NMR spectra confirming the purity and complete conversion of the starting materials into the product, as evidenced by the disappearance of the peak at −133 ppm in the product, can be found in SI Figure S3.[29] We assign this complete conversion to a purity of the surfactants synthesis close to 100 percent. Our synthetic processes consistently result in yields between 70 and 80 percent. The complete synthetic reaction can be found in SI Figure S1.

Pendant drop analysis

Interfacial tension measurements are conducted using the pendant drop method. Each solution sample is introduced into a 1 mL syringe and a 5 µL drop is analyzed using a Krüss DSA 30 drop shape analyzer. The Krüss ADVANCE software (v.1.6.2.0) facilitates drop creation and analysis.

Langmuir trough analysis

Using a Langmuir trough (KN2002, KSV Nima, Biolin Scientific, Finland), we determine the mean molecular area of the surfactants adsorbed on the air–water interface, approximating it to be similar to the area at the oil–water interface. To measure the surface pressure, a paper Wilhelmy plate is utilized. Before conducting the experiments, we ensure the cleanliness of the trough and Wilhelmy plate by confirming that the surface pressure remains below 0.3 mN/m when closing the barriers without adding any surfactant.

A solution containing 0.1% wt% of the surfactant is dissolved in the oil, and then 75 µL of this solution is gradually added to the water–air interface. To guarantee complete evaporation of the oil, we wait for 8 h before performing the experiments by closing the barriers at a speed of 5 mm/min. The minimum area occupied by the surfactant is identified as the region where the slope of the surface pressure against the mean molecular area exhibits for the first time a sharp increase.[21] The raw data can be found in SI Figure S10.

Fourier transform infrared spectroscopy

Each sample is purified and freeze-dried before it is analyzed. All spectra are recorded with a Spectrum 3 from PerkinElmer. A background spectrum is recorded before each sample.

Nuclear magnetic resonance

Samples are dissolved at 10 mg in 0.75 mL of hexafluorobenzene prior to analysis. All NMR spectra are recorded using a spectrometer operating at 400 MHz (Bruker AVANCE-400).

Microfluidic device fabrication

Masks for microfluidic devices are fabricated with soft lithography using the negative photoresist SU-8 that is patterned with photomasks following previously published methods.[30] To create the microfluidic devices, a mixture of PDMS and curing agent (Dow Corning, USA) at a weight ratio of 10:1 is poured into the master and polymerized overnight at 65°C. To prepare single water-in-oil drop emulsions, the channel surfaces are rendered fluorophilic by injecting a HFE7100-based solution containing 2% trichloro(1*H*,1*H*,2*H*,2*H*-perfluorooctyl)silane (Sigma-Aldrich, USA) into all channels for a duration of 10 min. The solution is removed from the channels and their surfaces are dried with compressed air. The efficacy of this surface treatment remains viable even after a three-month period following its initial preparation.

Production of single emulsions

Single emulsions are produced in a microfluidic flow focusing device with a channel cross section of 100 µm × 100 µm. To create single emulsions, the outer oil phase is introduced at a flow rate of 3000 µL/h using a syringe pump (Cronus Sigma 1000, LabHut, UK). Simultaneously, the inner phase is injected at a flow rate of 1000 µL/h using an identical syringe pump. A short piece of tubing is connected to the outlet of the microfluidic device and drops are collected in an oil-containing vial before they are transferred onto a microscopy slide to image them after 1 min, 1, 8, 48 h, and seven days of storage, as displayed in SI Figure S11. Drops were collected for 5 min, yielding approximately 100 µL of the aqueous phase that is transformed into drops. This process led to the production of over 200,000 individual drops.

HLB ratio: the HLB ratio was calculated using Equation 1, as previously reported.[31]

$$HLB = 20 \times \left({}^{M_h}/_{M} \right), \qquad 1$$

where M_h is the molecular weight of the hydrophilic block and M is the molecular weight of the whole molecule.

Acknowledgments

The authors would like to thank all the members of the Soft Materials Laboratory (SMaL) for fruitful discussions. They would also like to thank G. Dupont for her assistance while making single emulsions and Aurélien Bornet for his help with NMR. The work was financially supported by the bioinspired materials NCCR (205603).

Author contributions

G.D.A. and E.A. conceived the original idea for the study and G.D.A. performed all experiments. G.D.A. wrote the manuscript with support from E.A., who supervised the project. Both authors discussed the results and contributed to the final manuscript.

Funding

The work was financially supported by the bioinspired materials NCCR (205603).

Data availability

The data supporting this work are available on request from the corresponding author, E.A.

Conflict of interest

There are no conflicts to declare.

Supplementary information

The online version contains supplementary material available at https://doi.org/10.1557/s43577-024-00704-x.

References

1. E. Fredrick, P. Walstra, K. Dewettinck, *Adv. Colloid Interface Sci.* **153**, 30 (2010)
2. N. Sh. Stamkulov, K.B. Mussabekov, S.B. Aidarova, P.F. Luckham, *Colloids Surf. A Physicochem. Eng. Asp.* **335**, 103 (2009)
3. A.T. Florence, F. Madsen, F. Puisieux, *J. Pharm. Pharmacol.* **27**(6), 385 (1975)
4. Y. Chevalier, M.-A. Bolzinger, *Colloids Surf. A* **439**, 23 (2013)
5. M. Evans, I. Ratcliffe, P.A. Williams, *Curr. Opin. Colloid Interface Sci.* **18**(4), 272 (2013)
6. P. Raffa, D.A.Z. Wever, F. Picchioni, A. Broekhuis, *Chem. Rev.* **115**, 8504 (2015)
7. J. Bibette, F. Leal-Calderon, *Curr. Opin. Colloid Interface Sci.* **1**, 746 (1996)
8. T. Fujii, *Microelectron. Eng.* **61–62**, 907 (2002)
9. J.-C. Baret, *Lab Chip* **12**, 422 (2012)
10. C. Holtze, A.C. Rowat, J.J. Agresti, J.B. Hutchison, F.E. Angilè, C.H.J. Schmitz, S. Kõster, H. Duan, K.J. Humphry, R.A. Scanga, J.S. Johnson, D. Pisignano, D.A. Weitz, *Lab Chip* **8**(10), 1632 (2008)
11. O. Wagner, J. Thiele, M. Weinhart, L. Mazutis, D.A. Weitz, W.T.S. Huck, R. Haag, *Lab Chip* **16**(1), 65 (2016)
12. F. Junge, P.-W. Lee, A. Kumar Singh, J. Wasternack, M.P. Pachnicz, R. Haag, C.A. Schalley, *Angew. Chem. Int. Ed.* **62**(12), e202213866 (2023)
13. K.M. Horsman, J.M. Bienvenue, K.R. Blasier, J.P. Landers, *J. Forensic Sci.* **52**(4), 784 (2007)
14. J.-C. Baret, O.J. Miller, V. Taly, M. Ryckelynck, A. El-Harrak, L. Frenz, C. Rick, M.L. Samuels, J.B. Hutchison, J.J. Agresti, D.R. Link, D.A. Weitz, A.D. Griffiths, *Lab Chip* **9**(13), 1850 (2009)
15. L. Mazutis, J. Gilbert, W.L. Ung, D.A. Weitz, A.D. Griffiths, J.A. Heyman, *Nat. Protoc.* **8**(5), 870 (2013)
16. P.S. Dittrich, A. Manz, *Nat. Rev. Drug Discov.* **5**, 210 (2006)
17. J.L. Korner, E.B. Stephenson, K.S. Elvira, *Lab Chip* **20**, 1898 (2020)
18. F.W.Y. Chiu, H. Bagci, A.G. Fisher, A.J. deMello, K.S. Elvira, *J. Chem. Technol. Biotechnol.* **91**, 16 (2016)
19. P. Yager, T. Edwards, E. Fu, K. Helton, K. Nelson, M.R. Tam, B.H. Weigl, *Nature* **442**, 412 (2006)
20. M.T. Guo, A. Rotem, J.A. Heyman, D.A. Weitz, *Lab Chip* **12**, 2146 (2012)
21. K.S. Elvira, X.C. I Solvas, R.C. Wootton, A.J. Demello, *Nature Chem.* **5**, 905 (2013)
22. J.C. D’eon, S.A. Mabury, *Environ. Sci. Technol.* **41**, 4799 (2007)
23. X. Wu, C. Zhong, X. Lian, Y.R. Yang, *R. Soc. Open Sci.* **5**, 180610 (2018)
24. A. Chittofrati, D. Lenti, A. Sanguineti, M. Visca, C.M.C. Gambit, D. Senatrat, Z. Zhou, *Prog. Colloid Polym Sci.* **79**, 218 (1989)
25. G. De Angelis, N. Gray, V. Lutz-Bueno, E. Amstad, *Adv. Mater. Interfaces* **10**(13), 2202450 (2023)
26. C.-R. Li, N. Lutz-Bueno, V. Amstad, *Adv. Mater. Interfaces* **10**, 2300531 (2023)
27. W.D. Bancroft, W.D.V.J. Bancroft, *Phys. Chem.* **17**, 501 (1913)
28. Z. Che, T.N. Wong, N.-T. Nguyen, *Microfluid. Nanofluid.* **21**, 8 (2017)
29. S. Ursuegui, M. Mosser, A. Wagner, *RSC Adv.* **6**, 94942 (2016)
30. Y. Xia, G.M. Whitesides, *Angew. Chem. Int. Ed.* **37**, 550 (1998)
31. W.C. Griffith, *J. Soc. Cosmet. Chem.* **5**, 249 (1954) □

Publisher’s note