

## ELECTRONIC SUPPLEMENTARY INFORMATION

### A cyclodextrin surfactant for stable emulsions with accessible cavity for host-guest complexation

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## Experimental

### Chemicals

All chemicals were purchased from Acros Organics, Fischer Scientific GmbH, Schwerte, Germany, Aldrich, Sigma-Aldrich Chemie GmbH, Taufkirchen, Germany, Alfa Aesar, Alfa Aesar GmbH & Co KG, Karlsruhe, Germany, TCI Deutschland GmbH, Eschborn, Germany, Fluorochem, Chempur Feinchemikalien GmbH, Karlsruhe, Germany and used without further purification, if not stated otherwise. Moisture and air sensitive reactions were carried out in dried solvents. Therefore, glassware and molecular sieves (4 Å) were oven-dried at 120 °C, heat gun-dried under high vacuum and kept under argon atmosphere before adding solvents of analytical grade for drying. Standard SCHLENK techniques were used for reactions involving moisture and air sensitive reagents.

For the emulsion stability tests and surface tension measurements, hexadecane was purified from residual impurities by purification over aluminum oxide powder in a cleaned 100 ml glass flask (find the cleaning procedure below). The suspension was left to shake on an orbital shaker for 14 days and filtered afterwards.

### Dynamic light scattering (DLS)

Measurements were carried out on a *Nano ZS Zetasizer (Malvern Instruments)* at 25 °C and samples were prepared in disposable 1 mL semi-micro PMMA cuvettes (*BRAND*). Data analysis was performed with *Zetasizer Software Version 7.12 (Malvern Instruments)* and *OriginPro 9.6 (Origin)*. The hydrodynamic diameter was averaged over five measurements. Size distributions were obtained by applying a standard non-negative least square algorithm, which was implemented in the *Zetasizer Software* package.

### Emulsion stability test

After preparation of emulsions, the vials were placed in front of black graph paper and not moved for the duration of the test. At uneven intervals, photographic images were taken with a commercially available smartphone camera. The pictures were analyzed using ImageJ (version 1.40g). For the measurement of the height of the different emulsion phases, the scale was set against the dimension of the graphic paper in the background, which showed 1 cm x 1 cm squares divided into 10 equal 1 mm x 1 mm squares. Three measurements were carried out for each phase at the given time and the average height and standard deviation were calculated, which were then plotted against the time of observation.

## **Glassware**

All glassware was precleaned with Alconox detergent solution (Sigma Aldrich). After drying it was placed into concentrated sulfuric acid (98% p.a., Carl Roth) with NOCHROMIX (Godax Labs, Bethesda, MD, USA) for at least a day. Subsequently, the glassware was rinsed with copious amounts of ultrapure water thereafter it was dried in a stream of Argon (99.999% Westfalen Gas, Münster, Germany).

## **Light and fluorescence microscopy**

Microscopic images were recorded with a microscope *CKX41* (Olympus Deutschland GmbH, Hamburg, Germany). A *DX 20 I-FW* camera (Kappy opto-electronics GmbH, Gleichen, Germany) was used for recording and the obtained images were analyzed with *Stream Essentials* (version 1.9). For analyzation and insert of a scale bar *Image J* (version 1.50) was used.

## **Mass spectrometry**

Mass spectra were recorded with electrospray ionization (ESI) on a MicroTOF (Bruker Daltonics) and on a LTQ Orbitrap XL (ThermoFischer Scientific). Mass spectra were also recorded with Matrix assisted laser desorption/ionization (MALDI) on a Autoflex Speed MALDI-TOF (Bruker Daltonics).

## **NMR spectroscopy**

NMR spectroscopy was performed on a Bruker AV 300 and AV 400 (Bruker Corporation) instrument. All measurements were accomplished in deuterated solvents at room temperature. MestReNova 11.0 (Mestrelab Research S. L.) was used for data analysis. The chemical shifts were recorded in parts per million (ppm) and showed relative to the residual solvents signals. The coupling constants ( $J$ ) are noted in Hertz (Hz) and the following abbreviations for the description of multiplets were used: s = singlet, d = doublet, t = triplet, m = multiplet.

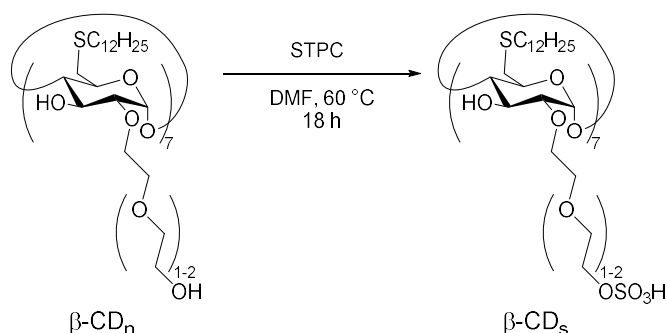
## **Sonication/Emulsification**

Emulsifications of aqu. solutions containing the surfactant (0.8 mM) and hexadecane (0.1 v%) were sonicated using a probe sonicator UP200St from Hielscher Ultrasonics GmbH (Teltow, Germany). The sonotrode (S26d7 from Hielscher Ultrasonics GmbH) was dipped approximately 1 cm into the solution and the sonication was carried out at 26 kHz for 1 min.

## Ultrapure Water

Ultrapure water with a resistance  $>18\text{ M}\Omega$  was obtained from Purelab UHQ water purification system (ELGA Labwater, Celle, Germany).

## Synthesis of $\beta\text{-CD}_s$



$\beta\text{-CD}_n$  (0.10 g, 0.03 mmol, 1.00 eq.) was synthesized as described,<sup>[1]</sup> transferred into a flask and dried overnight under high vacuum. The next day it was dissolved in dry DMF under inert conditions. Sulphur trioxide pyridine complex (STPC, 178.0 mg, 1.12 mmol, 5.0 eq. for each OH-group) was dissolved in DMF (dry, 10 mL) in an inert atmosphere and dropwise added to the amphiphilic cyclodextrin  $\beta\text{-CD}_n$ . The reaction mixture was heated to 60 °C and stirred for 18 h. Then, deionized water was added to quench the reaction and 1 M NaOH was added until pH 11 was reached. The solvent was removed and the yellowish gel was dissolved in water and purified by dialysis (MWCO=500-1000 Da) in sat. aqu. NaCl solution and deionized water for 2 d each solvent. After evaporation of the solvent, the product  $\beta\text{-CD}_s$  was obtained as a yellowish gel.

**Yield:** 96%

**<sup>1</sup>H-NMR** (400 MHz, 343 K, D<sub>2</sub>O)  $\delta$  = 5.63 (s, 7H, H1), 4.76 - 3.84 (m, 85H, H2 - H5 and OCH<sub>2</sub>CH<sub>2</sub>O), 3.56 (s, 14H, H6), 3.12 (s, 14H, SCH<sub>2</sub>), 2.10 (s, 14H, CH<sub>2</sub>), 1.80 (s, 120H, CH<sub>2</sub>), 1.37 (s, 21H, CHC) ppm.

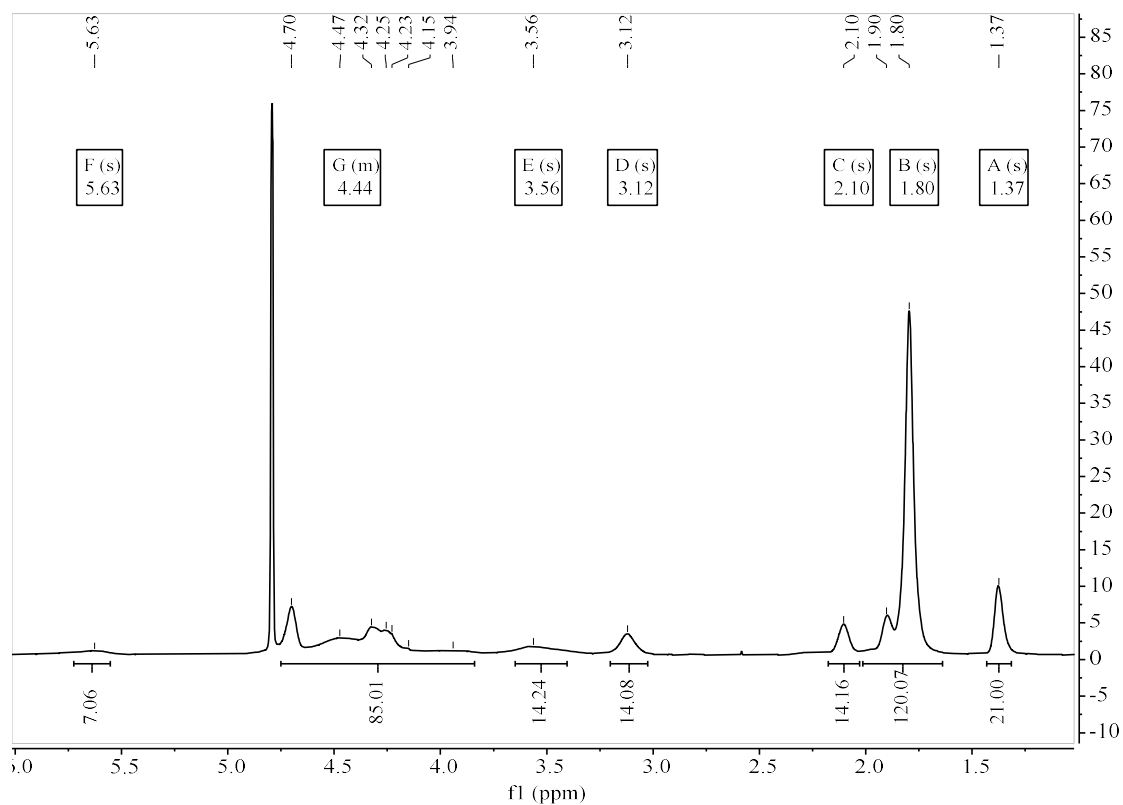
**<sup>13</sup>C-NMR** (75 MHz, 343 K, D<sub>2</sub>O)  $\delta$  = 81.1 (OSOCH at C3, C2, C4), 70.3 - 69.5 (C3, C5, CH<sub>2</sub>O), 68.1 (CH<sub>2</sub>O), 34.0 - 32.3 (SCH<sub>2</sub>, C6), 30.2 (CH<sub>2</sub>), 22.9 (CHCCH<sub>2</sub>), 14.2 (CHC) ppm.

**MS (m/z)** (MALDI, DHB (H<sub>2</sub>O/ACN)): Calculated for [(C<sub>152</sub>H<sub>290</sub>O<sub>50</sub>S<sub>10</sub>)Na<sub>2</sub>]<sup>2+</sup>: 3283.7; found: 3283.3 (3xsulfated). Calculated for [(C<sub>152</sub>H<sub>285</sub>O<sub>53</sub>S<sub>11</sub>)Na<sub>5</sub>]<sup>5+</sup>: 3426.6; found: 3426.9

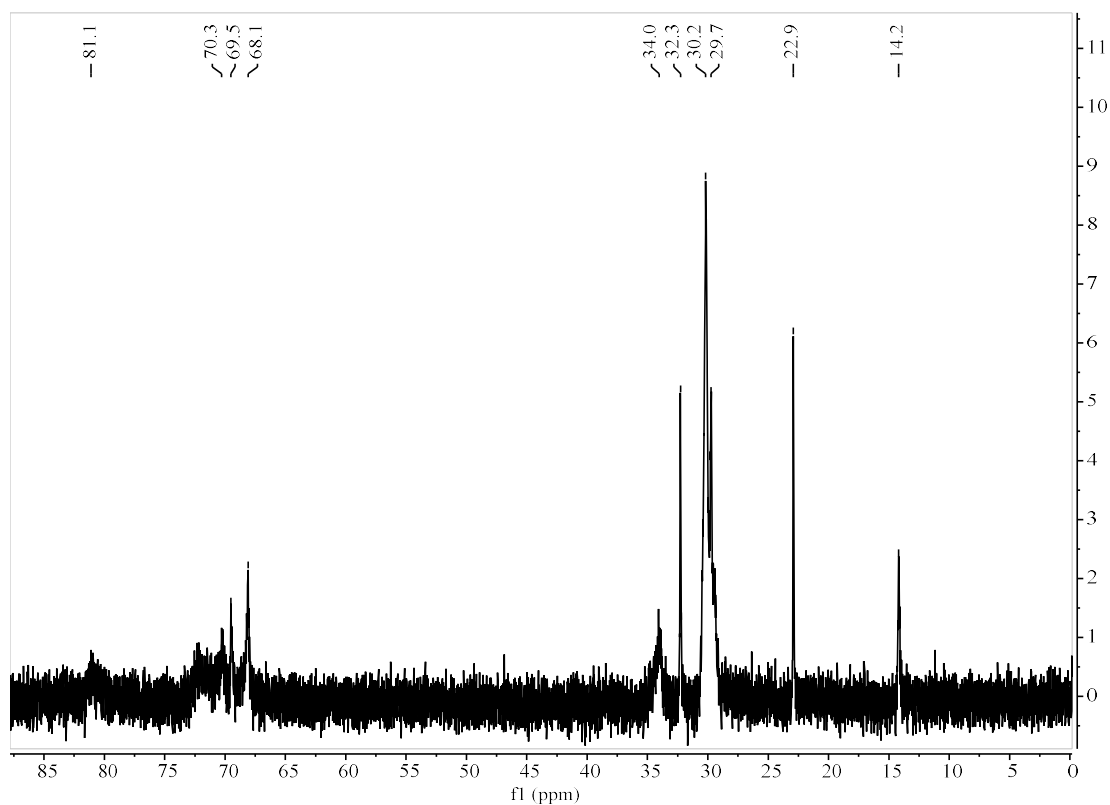
(4x sulfated). Calculated for  $[(C_{152}H_{285}O_{56}S_{12})Na_6]^{6+}$ : 3530.6; found: 3530.2 (5x sulfated).

Calculated for  $[(C_{152}H_{285}O_{59}S_{13})Na_5]^{5+}$ : 3587.5; found: 3587.8 (6x sulfated).

## NMR spectra of $\beta$ -CD<sub>s</sub>

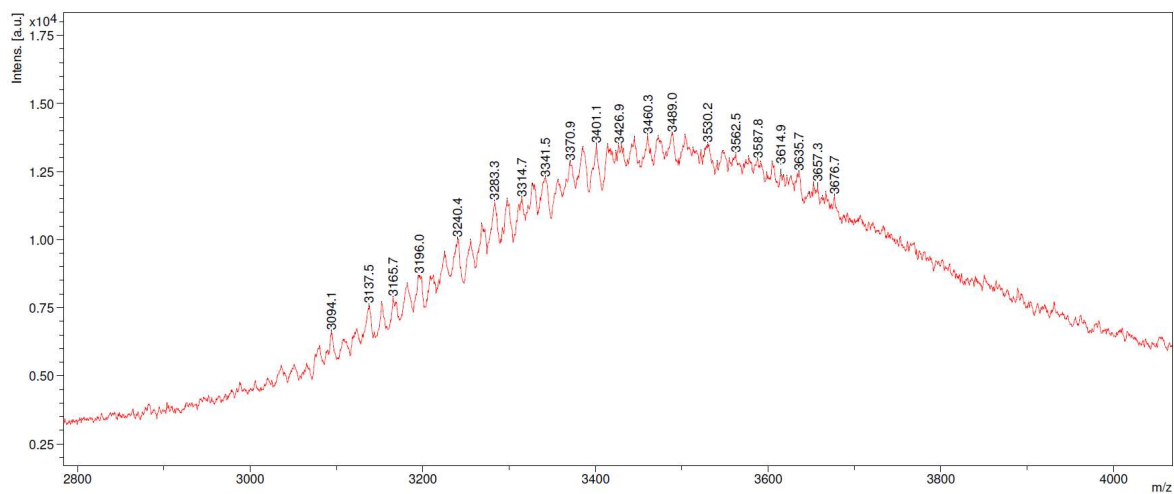


**Figure S1:** <sup>1</sup>H-NMR spectrum of β-CD<sub>s</sub> measured in D<sub>2</sub>O at 343 K and 400 MHz.



**Figure S2:**  $^{13}\text{C}$ -NMR spectrum of  $\beta$ -CDs measured in  $\text{D}_2\text{O}$  at 343 K and 75 MHz.

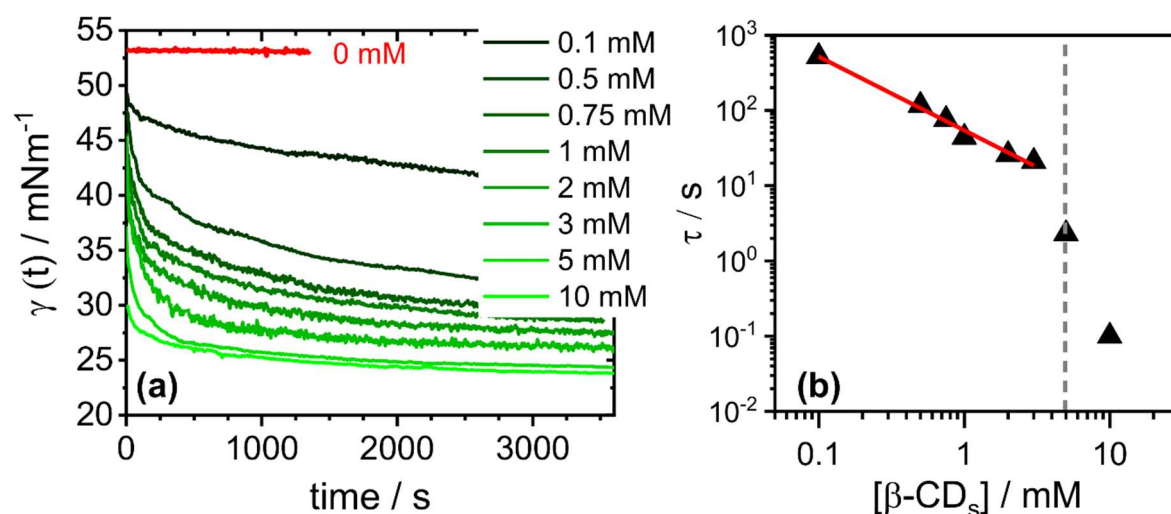
### Mass spectrum of $\beta$ -CD<sub>s</sub>



**Figure S3:** MALDI-TOF-MS spectrum of  $\beta$ -CD<sub>s</sub> measured using a DHB matrix ( $\text{H}_2\text{O}/\text{AcCN}$ ).

## Analysis of the interface tension and surfactant adsorption

The dynamic interfacial tension  $\gamma(t)$  of  $\beta$ -CD<sub>s</sub> at the hexadecane-water interface was recorded with a PAT-1M (Sinterface, Germany) tensiometer. For that, we have applied the emerging bubble technique where a hexadecane-droplet was placed into a cuvette filled with the aqueous phase. To ensure the purity of the hexadecane and the aqueous phase, a test experiment was performed at the start of each measurement day using ultrapure water without surfactant in order to make sure that the surface tension was around 53 mN/m.<sup>[3]</sup>



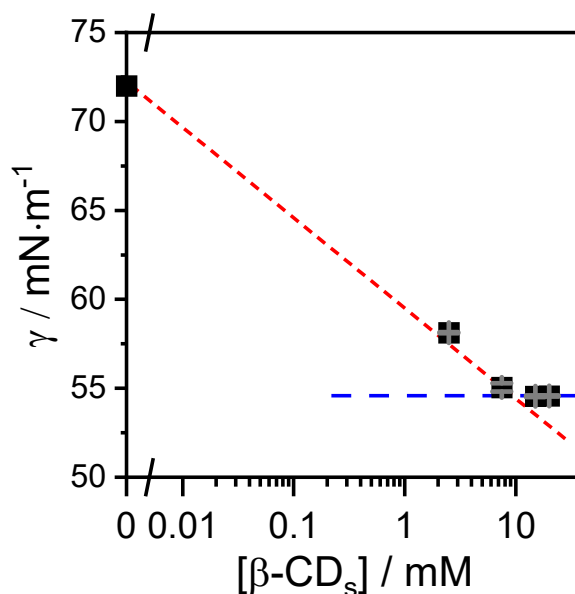
**Figure S4:** (a) Dynamic interface tension of the hexadecane-water interface as a function of time and for different  $\beta$ -CD<sub>s</sub> concentrations as indicated in the figure. (b) Characteristic adsorption time as defined in the text below in dependence of the  $\beta$ -CD<sub>s</sub> concentration. For (b) the results in (a) have been analyzed.

In addition, the dynamic interface tension for a neat interface without surfactant was monitored as a function of time and did not show any noticeable decrease in interface tension over time, which we take as further evidence for the purity of the oil and the aqueous phases.

To gain information on the surface excess of  $\beta$ -CD<sub>s</sub> at the hexadecane-water interface, the interface tension after 60 min was plotted against the logarithmic concentration of  $\beta$ -CD<sub>s</sub> and a linear regression was carried out in the declining regime of the surface tension until the CMC that we estimate to be at 5 mM (see main text). Using the slope  $m$  and the Gibbs-isotherm  $\Gamma = -\frac{1}{(z+1)RT} \cdot \frac{d\gamma}{d \ln(c)} = -\frac{m}{(z+1)RT}$ , where  $R$  is the universal gas constant,  $z$  the number of counterions and  $T$  the temperature in K. Taking into account that the  $\beta$ -CD<sub>s</sub> moieties in our experiments had 7 sulfate groups we were using  $z=7$  and obtain a maximal surface excess  $\Gamma$  of 0.12 molecules/nm<sup>2</sup> (816 Å<sup>2</sup>/molecule) which is discussed in detail in the main text.

In order to further corroborate our conclusion on the CMC of  $\beta$ -CD<sub>s</sub> at 5 mM, we have determined the characteristic time  $\tau$  of adsorption, which is a function of concentration, but also of the diffusion coefficient  $D$ .  $D$  is necessarily different for monomers and micelles and, consequently, an analysis of characteristic adsorption time can be useful.  $\tau$  is defined as the time where half of the maximum change in the interface tension from the neat interface tension is reached at a given concentration  $[\beta\text{-CD}_s]$ . Accordingly, we can write  $\gamma(\tau) = \frac{\gamma_0 - \gamma_{eq}([\beta\text{-CD}_s])}{2}$  where  $\gamma_0$  and  $\gamma_{eq}$  are the equilibrium interface tensions of the neat interface and the surfactant modified interface. Close inspection of Figure S4b clearly shows that for concentrations  $<5$  mM,  $\tau$  obeys a linear scaling law in the log-log plot that is similar to classical surfactants, while for concentration  $\geq 5$  mM a drastic change in  $\tau$  is observed and can be associated to a transition from predominant monomeric to micellar adsorption.

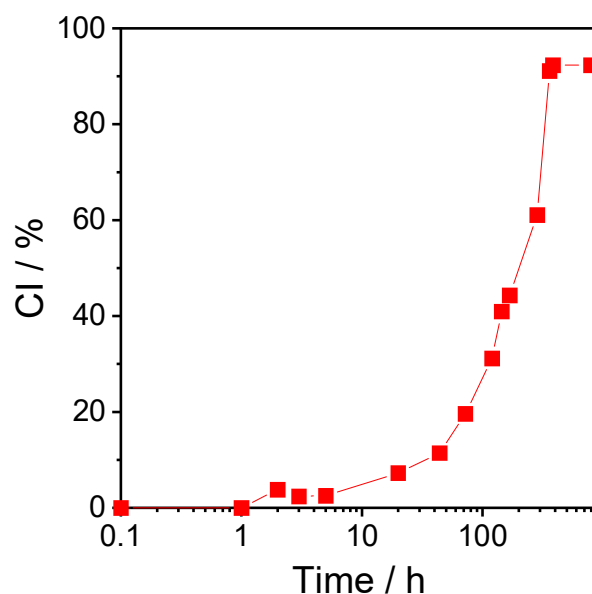
For dynamic surface tension measurements at the air-water-interface, a pendant drop tensiometer (DSA100, Krüss, Germany) was used where an aqueous drop of  $\beta$ -CD<sub>s</sub> with different concentrations was formed at the end of a syringe cannula and a CCD camera monitored its shape. Through the use of image analysis and the Young–Laplace equation, the surface tension was determined from the drop shape as a function of time until equilibrium was reached. In order to avoid strong evaporation, the gas phase around the pendant drop was saturated by use of a water-filled cuvette.



**Figure S5:** Equilibrium surface tension values of  $\beta$ -CD<sub>s</sub> at the air-water-interface. The dashed blue line indicates the interface tension above the CMC.

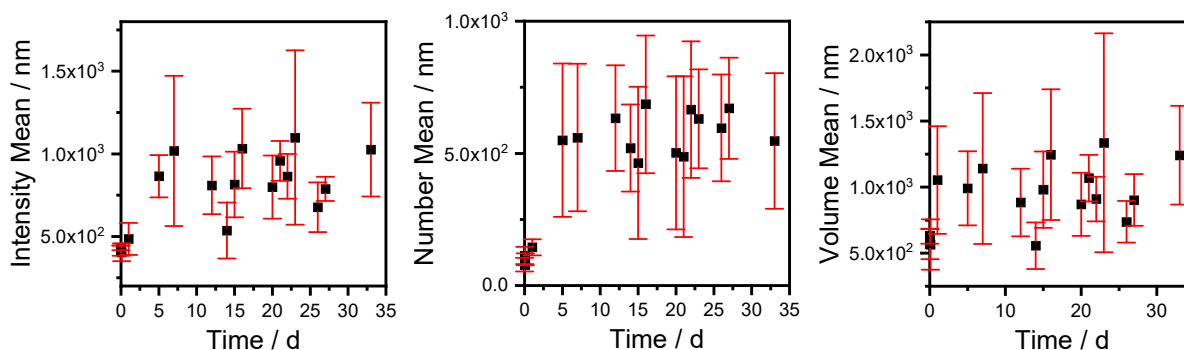


## Analysis of creaming behavior



**Figure S6:** Calculated Creaming Index (CI) plotted against the time in percent.

The Creaming Index (CI) was calculated using the formula  $CI = 100 \cdot \frac{H_S^t}{H_E^0}$ , where  $H_S^t$  is the height of the serum phase at a given time and  $H_E^0$  is the initial height of the emulsion at  $t = 0$ .<sup>[2]</sup>



**Figure S7:** DLS analysis of an emulsion containing  $\beta$ -CDs (0.8 mM) and hexadecane (0.1 v%) over time. For the DLS analysis dilutions of the emulsions (10v% in MQ) were prepared and measured. Plots of the average hydrodynamic diameters calculated through five independent measurements: Intensity (left), number (middle) and volume weighed (right) results.

## References

- [1] a) B. J. Ravoo, R. Darcy, *Angew. Chem. Int. Ed.* 2000, **39**, 4324–4326; b) P. Falvey et al., *Chem. Eur. J.* 2005, **11**, 1171–1180;
- [2] D. J. McClements, *Crit. Rev. Food Sci. Nutr.* 2007, **47**, 611–649.
- [3] R. Aveyard, D. A. Haydon, *Trans. Faraday Soc.* 1965, **61**, 2255–2261.