SUPPLEMENTARY INFORMATION

The polyphenol EGCG inhibits amyloid formation less efficiently at phospholipid interfaces than in bulk solution

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Supplementary Table S1. Fit parameters for fits of SFG spectra of IAPP-DPPG

time (min)	Ampl. 1 (a.u.)	Freq. 1 (cm^{-1})	FWHH 1 (cm^{-1})	Ampl. 2 (a.u.)	Freq. 2 (cm^{-1})	FWHH 2 (cm^{-1})	Ampl. 3 (a.u.)	Freq. 3 (cm^{-1})	FWHH 3 (cm^{-1})
14	20.4	1650.8	40.7	6.1	1670.5	32.8	16.9	1732.9	41.2
82	18.6	1650.8	40.7	10.3	1670.5	32.8	17.1	1732.9	41.2
153	23.8	1650.8	40.7	8.1	1670.5	32.8	11.1	1732.9	41.2
230	16.7	1650.8	40.7	10.3	1670.5	32.8	18.9	1732.9	41.2
316	21.1	1650.8	40.7	11.6	1670.5	32.8	16.2	1732.9	41.2
588	12.7	1650.8	40.7	16.6	1670.5	32.8	16.4	1732.9	41.2
1391	6.8	1650.8	40.7	18.9	1670.5	32.8	16.4	1732.9	41.2
1530	5.2	1650.8	40.7	19.7	1670.5	32.8	17.7	1732.9	41.2

For all fits, the non-resonant amplitude and phase were 0.53 and -1.24, respectively. The peak positions and the full width at half height (FWHH) are linked for the eight SFG spectra measured at different time points.

Supplementary Table S2. Fit parameters for fits of SFG spectra of IAPP-DPPG with EGCG

time (min)	Ampl. 1 (a.u.)	Freq. 1 (cm^{-1})	FWHH 1 (cm^{-1})	Ampl. 2 (a.u.)	Freq. 2 (cm^{-1})	FWHH 2 (cm^{-1})	Ampl. 3 (a.u.)	Freq. 3 (cm^{-1})	FWHH 3 (cm^{-1})
16	30.2	1652.3	36.2	11.3	1670.2	36.4	16.6	1730	47.8
98	31.5	1652.3	36.2	15.0	1670.2	36.4	18.8	1730	47.8
166	33.1	1652.3	36.2	14.5	1670.2	36.4	17.0	1730	47.8
384	28.8	1652.3	36.2	23.3	1670.2	36.4	14.7	1730	47.8
1221	28.4	1652.3	36.2	20.6	1670.2	36.4	13.3	1730	47.8
1421	25.0	1652.3	36.2	25.4	1670.2	36.4	17.5	1730	47.8
1606	24.2	1652.3	36.2	25.4	1670.2	36.4	19.4	1730	47.8

For all fits, the non-resonant amplitude and phase were 0.28 and -1.14, respectively. The peak positions and the full width at half height (FWHH) are linked for the seven SFG spectra measured at different time points.

Supplementary Table S3. Fit parameters for fits of SFG spectra of IAPP in absence of DPPG

time (min)	Ampl. 1 (a.u.)	Freq. 1 (cm^{-1})	FWHH 1 (cm^{-1})	Ampl. 2 (a.u.)	Freq. 2 (cm^{-1})	FWHH 2 (cm^{-1})
14	30.03	1645.4	28.3	8.2	1663.3	26.7
58	25.4	1645.4	28.3	4.1	1663.3	26.7
106	24.8	1645.4	28.3	1.7	1663.3	26.7
183	23.7	1645.4	28.3	3.0	1663.3	26.7
248	30.1	1645.4	28.3	2.0	1663.3	26.7
1336	27.8	1645.4	28.3	9.1	1663.3	26.7
1493	34.2	1645.4	28.3	5.3	1663.3	26.7
1656	28.7	1645.4	28.3	8.3	1663.3	26.7

For all fits, the non-resonant amplitude and phase were 0.41 and -1.8, respectively. The peak positions and the full width at half height (FWHH) are linked for the eight SFG spectra measured at different time points.

Supplementary Table S4. Fit parameters for fits of SFG spectra of IAPP fibrils incubated with 1 μM EGCG for different times.

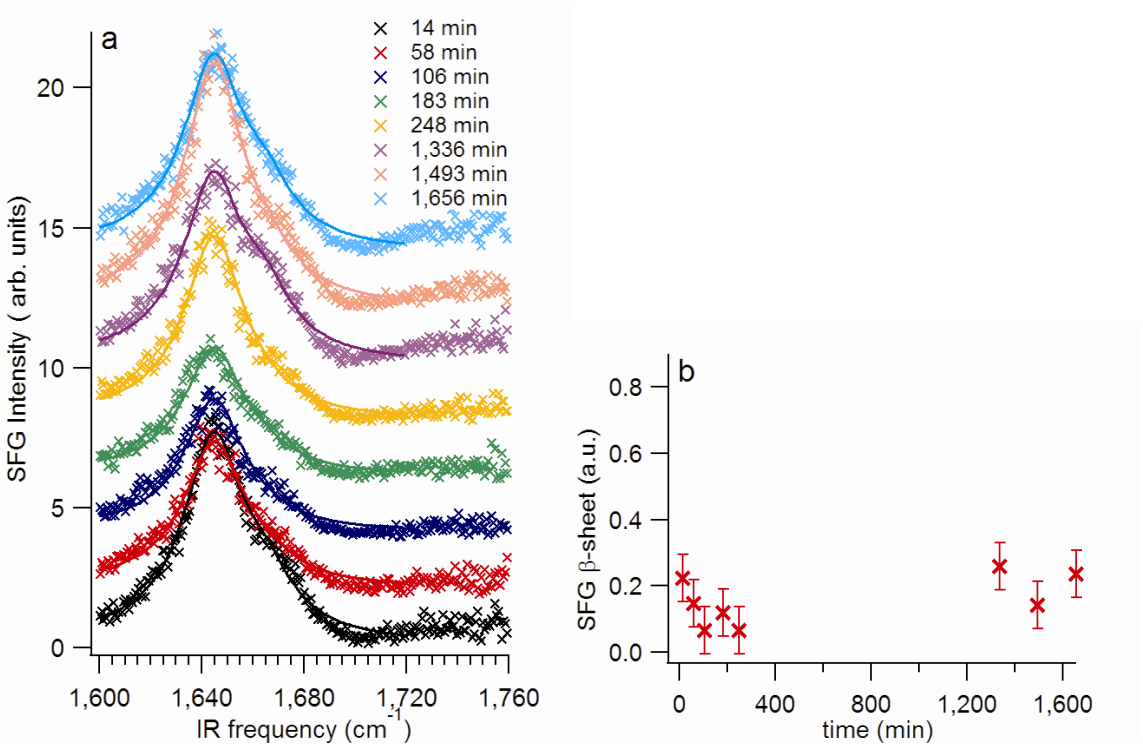
time (min)	Ampl. 1 (a.u.)	Freq. 1 (cm^{-1})	FWHH 1 (cm^{-1})	Ampl. 2 (a.u.)	Freq. 2 (cm^{-1})	FWHH 2 (cm^{-1})	Ampl. 3 (a.u.)	Freq. 3 (cm^{-1})	FWHH 3 (cm^{-1})
14	10.9	1648.7	30.2	45.2	1667.8	38.0	19.7	1725.5	37.7
120	17.3	1648.7	30.2	42.6	1667.8	38.0	16.0	1725.5	37.7
2880	6.6	1648.7	30.2	44.3	1667.8	38.0	17.9	1725.5	37.7

For all fits, the non-resonant amplitude and phase were 0.64 and -0.81, respectively. The peak positions and the full width at half height (FWHH) are linked for the three SFG spectra measured at different time points.

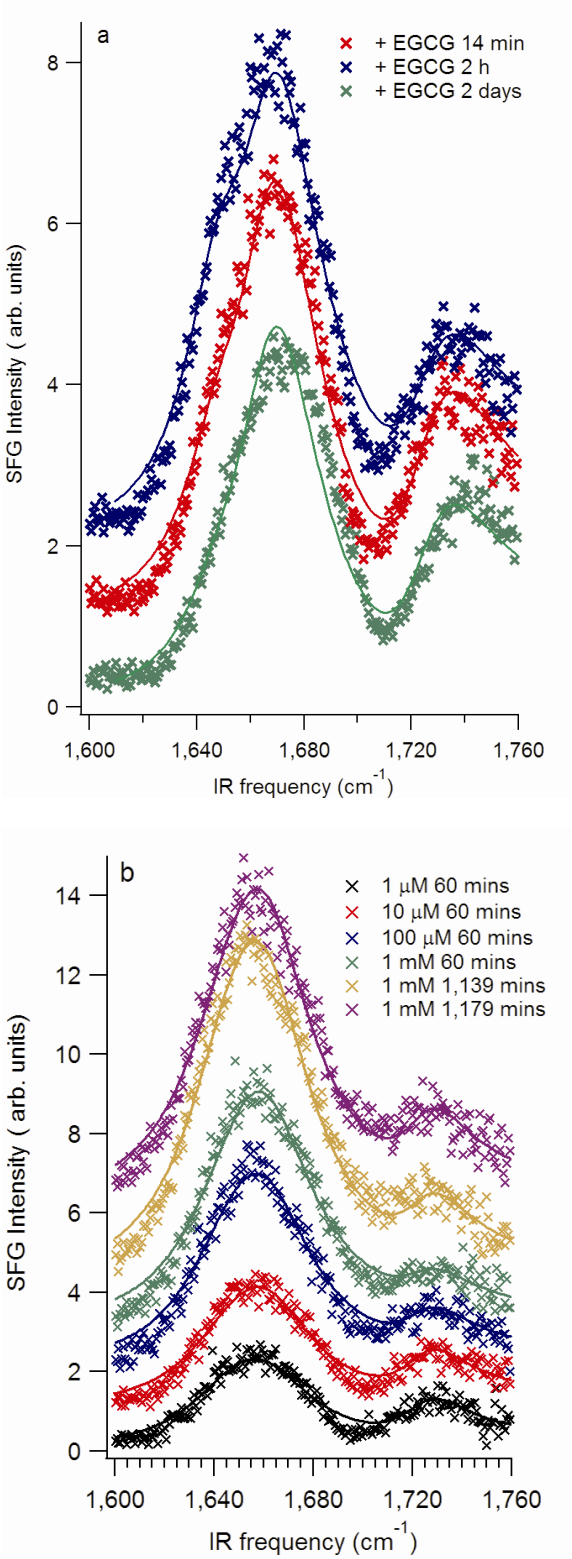
Supplementary Table S5. Fit parameters for fits of SFG spectra of IAPP fibrils incubated with EGCG at different concentrations and for different times.

[EGCG] (mM)	time (min)	Ampl. 1 (a.u.)	Freq. 1 (cm^{-1})	FWHH 1 (cm^{-1})	Ampl. 2 (a.u.)	Freq. 2 (cm^{-1})	FWHH 2 (cm^{-1})	Ampl. 3 (a.u.)	Freq. 3 (cm^{-1})	FWHH 3 (cm^{-1})
0.001	60	10.5	1644.4	34.8	17.3	1661.4	43.4	9.3	1724.4	34.8
0.01	60	11.1	1644.4	34.8	22.5	1661.4	43.4	9.9	1724.4	34.8
0.1	60	15.2	1644.4	34.8	29.4	1661.4	43.4	8.1	1724.4	34.8
1	60	15.2	1644.4	34.8	34.7	1661.4	43.4	6.3	1724.4	34.8
1	1139	20.4	1644.4	34.8	41.4	1661.4	43.4	10.3	1724.4	34.8
1	1179	17.4	1644.4	34.8	41.5	1661.4	43.4	11.8	1724.4	34.8

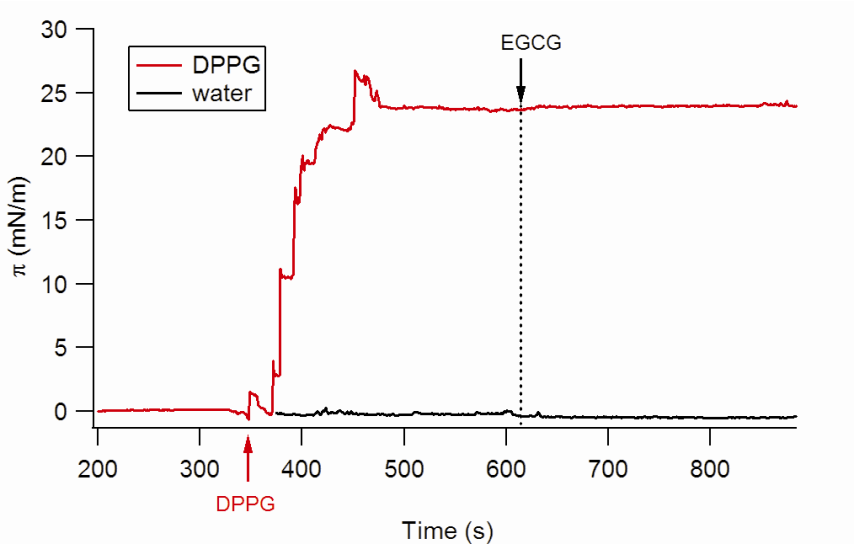
For all fits, the non-resonant amplitude and phase were 0.37 and -0.90, respectively. The peak positions and the full width at half height (FWHH) are linked for the six SFG spectra.



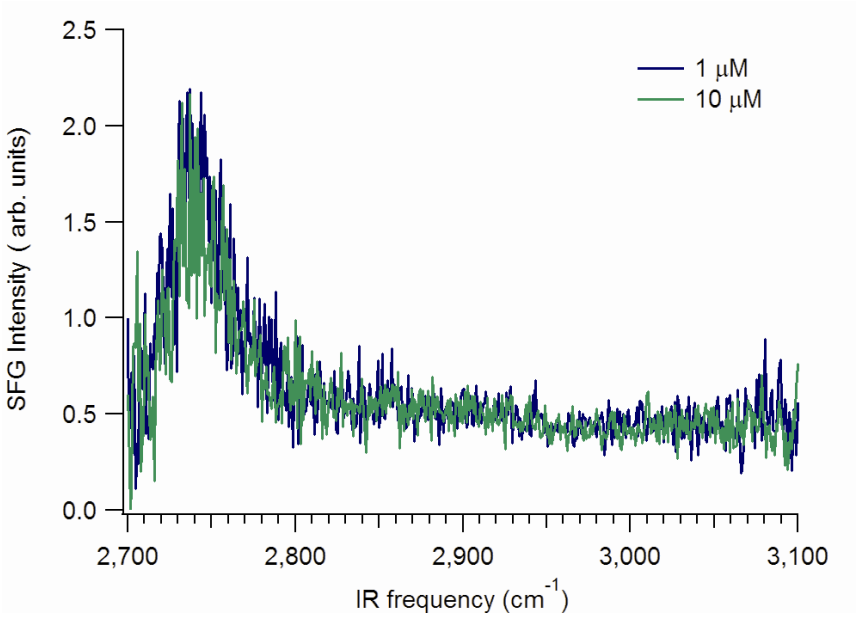
Supplementary Fig. S1. (a) SFG spectra of 1 μM hIAPP at the air/water interface in absence of DPPG as a function of time. The solid lines represent the fits to the data. (b) The relative β-sheet intensity from SFG as a function of time.



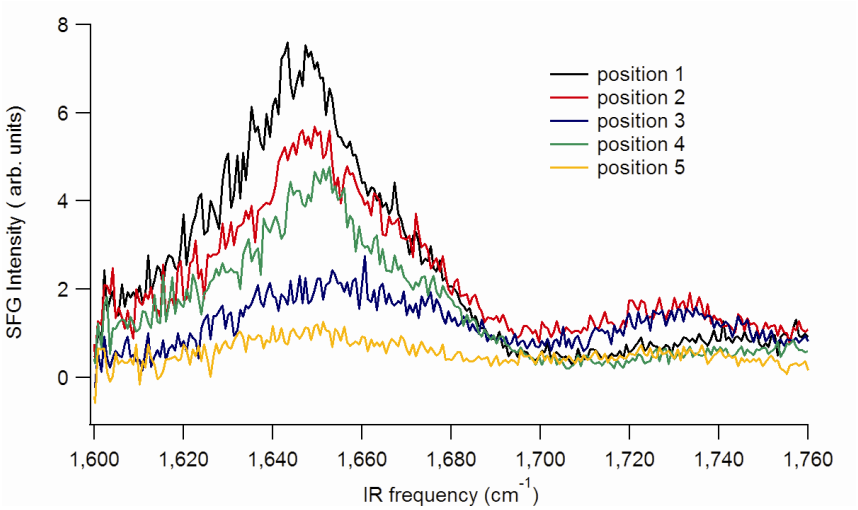
Supplementary Fig. S2. SFG spectra and fits of incubation of 1 µM hIAPP fibrils at the air/DPPG/water interface (a) with 1 µM EGCG for three different times, and (b) of incubation with different concentrations of EGCG at the air/DPPG/water interface. The solid lines represent the fits to the data.



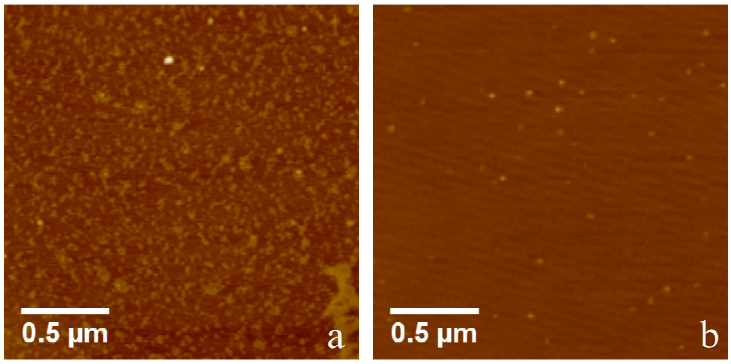
Supplementary Fig. S3. Change in surface pressure upon the addition of EGCG (1 µM final concentration) to a water interface (black) or DPPG interface (red). The dotted line indicates the time when EGCG is added. The black trace has been given an offset in the x-direction such that the time of EGCG injection matches that of the red trace.



Supplementary Fig. S4. SFG spectra of EGCG at 1 and 10 μM in D_2O show the absence of any EGCG signal. The signal at 2,740 cm^{-1} stems from the free OD of surface water molecules.

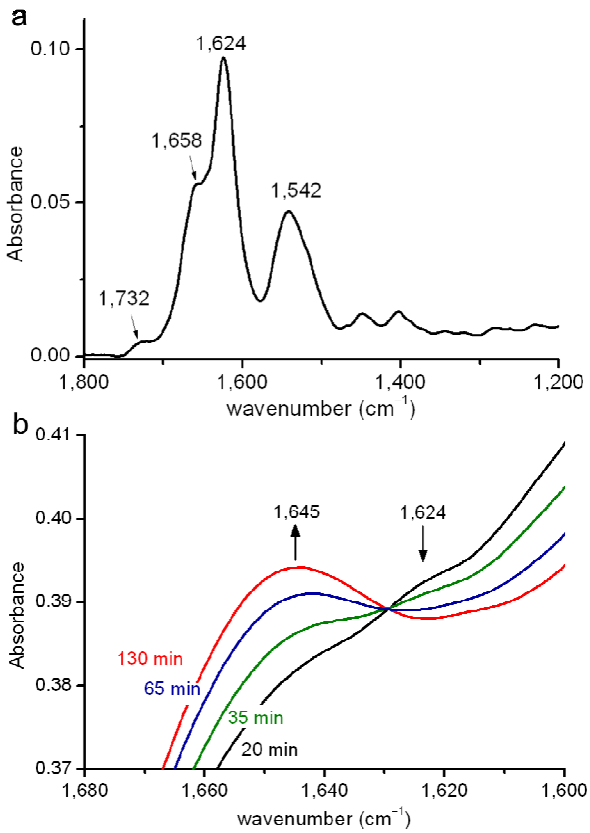


Supplementary Fig. S5. SFG spectra showing spatial heterogeneity of a hIAPP/DPPG interface. The spectra were measured at 5 different positions. The VSFG signals arise from an area with a size in the order of hundreds of µm. This is a much larger length scale than the scale seen in AFM images, in which a square of 5x5 µm is probed.



Supplementary Fig. S6. AFM images of hIAPP fibrils formed at the lipid-water interface before (a) and after (b) incubation with 100 µM EGCG for 1 hr.

Experimental procedure of Disaggregation of fibrils disengaged from the lipid-water interface by EGCG: To investigate the effect of EGCG on interface-fibrils in the absence of lipids, fibrils were formed at the lipid-water interface as described in the 'Experimental Section: Preparation of solutions and monolayers.' To exclude side-effects of potential formation of hIAPP fibrils in the bulk below the lipid-water interface, the bulk solution was removed after incubation over night. The lipid-protein mixture was collected, diluted and extensively washed with buffer to remove the lipids. Fibrils were concentrated by ultrafiltration using centrifugal filters with molecular weight cutoff of 10 kDa (Amicon Ultra-4, Millipore, Cork, Ireland). AFM samples were prepared before and after incubation with 100 µM EGCG for 1 hr, as described in the 'Experimental Section: Atomic Force Microscopy (AFM)' for analysis of samples from the ThT test.



Supplementary Fig. S7. FT-IR absorption spectra of hIAPP. (a) ATR spectrum of a dry amyloid film, showing vibrational bands at 1,732 cm^{-1} (C=O stretching vibrations of the C-terminal lysine), 1,658 and 1,624 cm^{-1} (amide I band corresponding to unordered/ helical structures and β-sheet structure, respectively) and 1,542 cm^{-1} (amide II band). (b) Transmission FT-IR spectra of hIAPP and EGCG in a 1:1 molar ratio in D_2O, in the spectral region of the amide I band. Spectra were taken 20 min (red line), 35 min (green line), 65 min (blue line) and 130 min (black line) after mixing hIAPP and inhibitor. Over time, the band at 1624 cm^{-1} vanishes; a new band appears around 1,645 cm^{-1}; both changes are indicated by the two black arrows. The background absorption is due to a broad D_2O combination band centered at 1555 cm^{-1}.