Supporting Information

Probing the complex loading dependent structural changes in ultra-high drug loaded polymer micelles by small angle neutron scattering

Benedikt Sochor[1,✢], Özgür Düdükcü[1,✢], Michael M. Lübtow[2], Bernhard Schummer[3], Sebastian Jaksch[4,*], Robert Luxenhofer[2,5*]

[1]*Chair of X-Ray Microscopy, Department of Physics and Astronomy, University Würzburg, Campus Hubland Nord, Josef-Martin-Weg 63, 97074 Würzburg, Germany*

[2] *Functional Polymer Materials, Chair for Advanced Materials Synthesis, Department of Chemistry and Pharmacy and Bavarian Polymer Institute, University of Würzburg, Röntgenring 11, 97070 Würzburg, Germany*

[4] *Fraunhofer Institute for Integrated Circuits, X-Ray Development Center EZRT, Flugplatzstraße 75, 90768 Fürth, Germany*

[3] *Forschungszentrum Jülich GmbH, Jülich Center for Neutron Science (JCNS) at Heinz Maier-Leibnitz Zentrum, Lichtenberstraße 1, 85747 Garching, Germany*

[5] *Soft Matter Chemistry, Department of Chemistry, Helsinki University, 00014 Helsinki, Finland*

✢ authors contributed equally
*correspondence to: robert.luxenhofer@uni-wuerzburg.de, s.jaksch@fz-juelich.de

17 pages, 8 Figures

Densimetric data

A-pBuOx-A/CUR

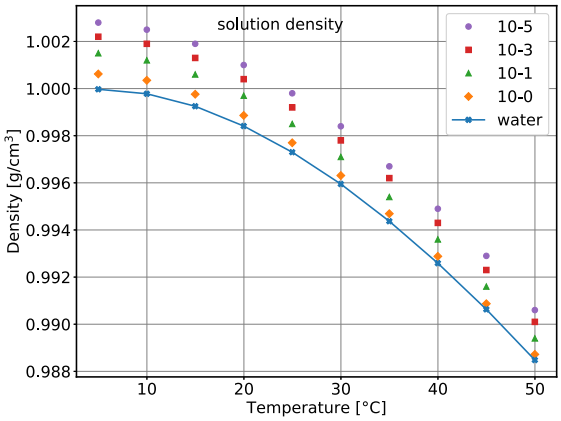


Figure S1: solution density of 10 mg/ml A-pBuOx-A mixed with CUR (concentrations: 1-5 mg/ml) in H_2O.

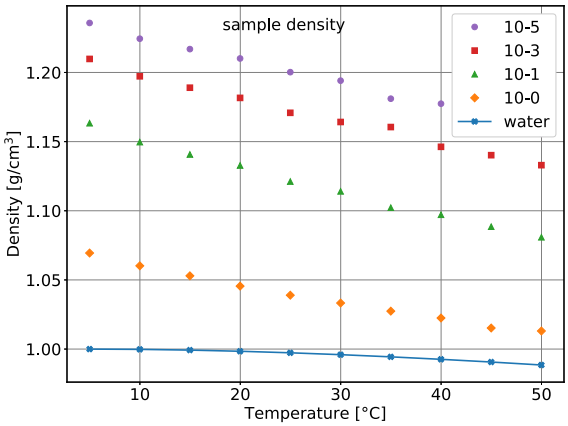


Figure S2: combined density of A-pBuOx-A and CUR after water content subtraction.

A-pBuOzi-A/CUR

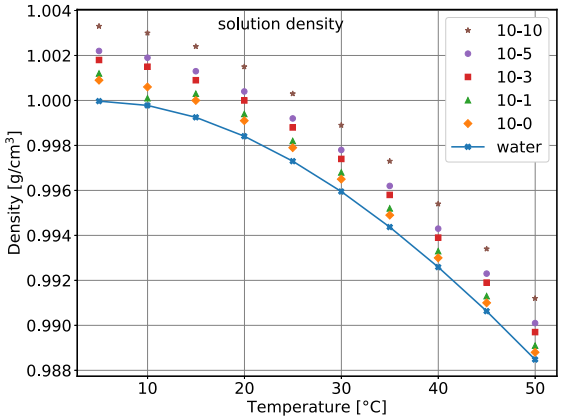


Figure S3: solution density of 10 mg/ml A-pBuOzi-A mixed with CUR (concentrations: 1-10 mg/ml) in H_2O.

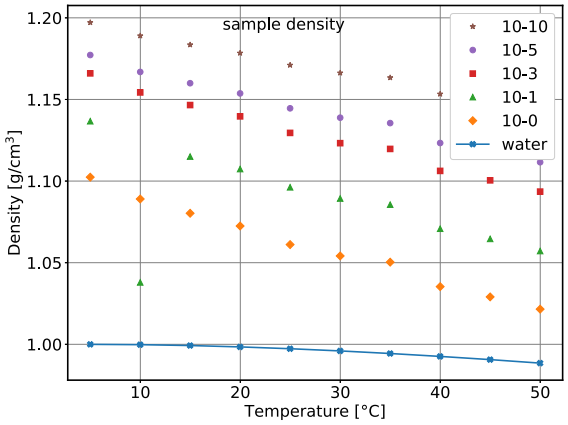


Figure S4: combined density of A-pBuOzi-A and CUR after water content subtraction.

A-pPrOzi-A/CUR

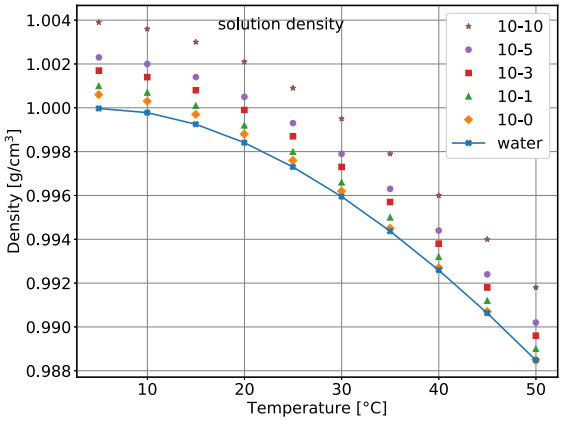


Figure S5: solution density of 10 mg/ml A-pPrOzi-A mixed with CUR (concentrations: 1-10 mg/ml) in H_2O.

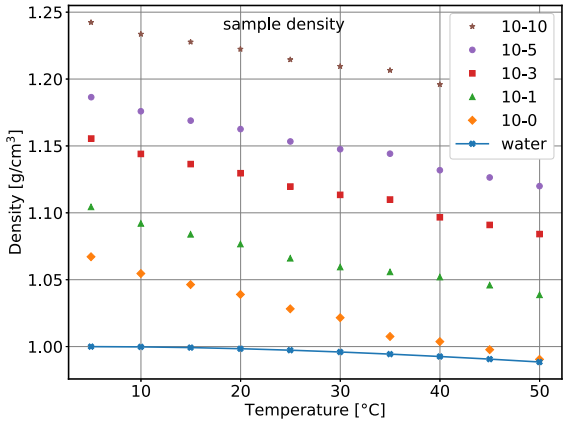


Figure S6: combined density of A-pPrOzi-A and CUR after water content subtraction.

Small-Angle-Neutron-Scattering (SANS)

Model Justification

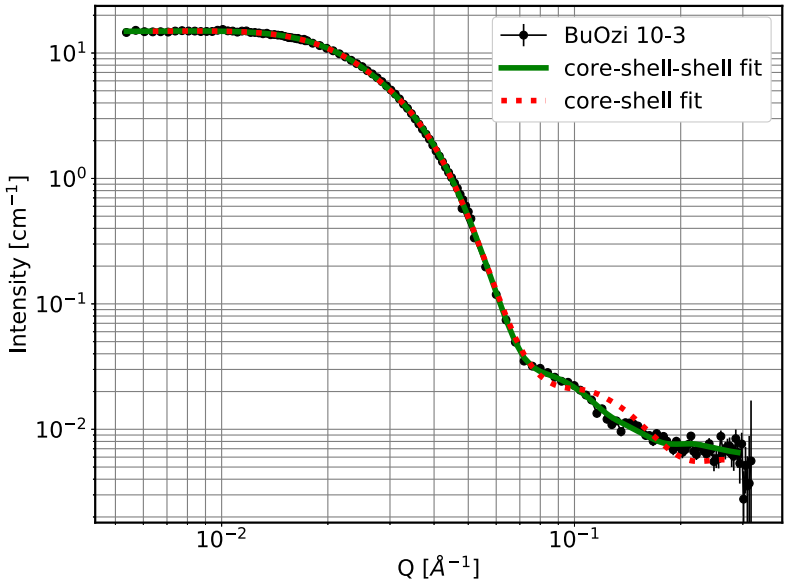


Figure S7:Comparison of the fit using a core-shell (red and dashed line) and core-shell-shell sphere model (green and solid line) on basis of the 10-3 data of A-pBuOzi-A (black spheres).

To clarify, which model should be used for fitting, the SANS data of A-pBuOzi-A mixed with different concentrations of CUR was analyzed more systematically. For each A-pBuOzi-A/Cur sample, both core-shell sphere and core-shell-shell sphere models were used for fitting. In general, the core-shell-shell model produced the better looking fits. For quantification the

$$\chi^2 = \sum_{i}^{N} \left(\frac{I_{model} - I_{experiment}}{\sigma_i} \right)^2$$

of each fit was calculated with I_{model} being the calculated model Intensities, $I_{experiment}$ the experimental data and σ the experimental errors. A χ^2-value of 1 indicates a perfect fit, while lower χ^2 indicate a numerically favorable fit result. For A-pBuOzi-A a clear trend towards a core-shell-shell model is visible (see Figure 8).

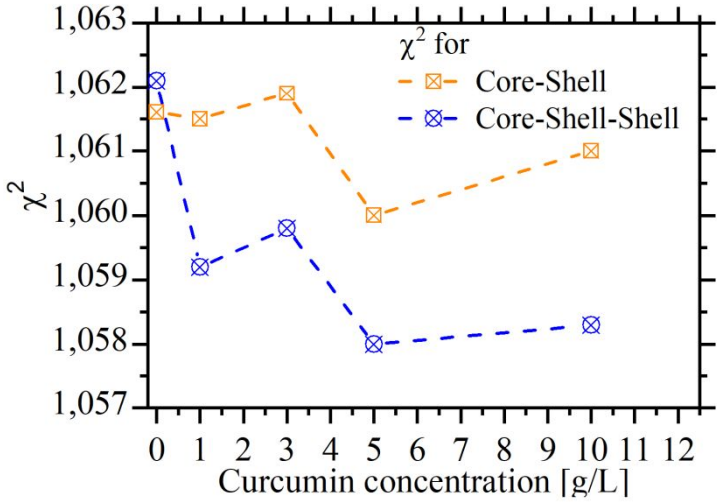
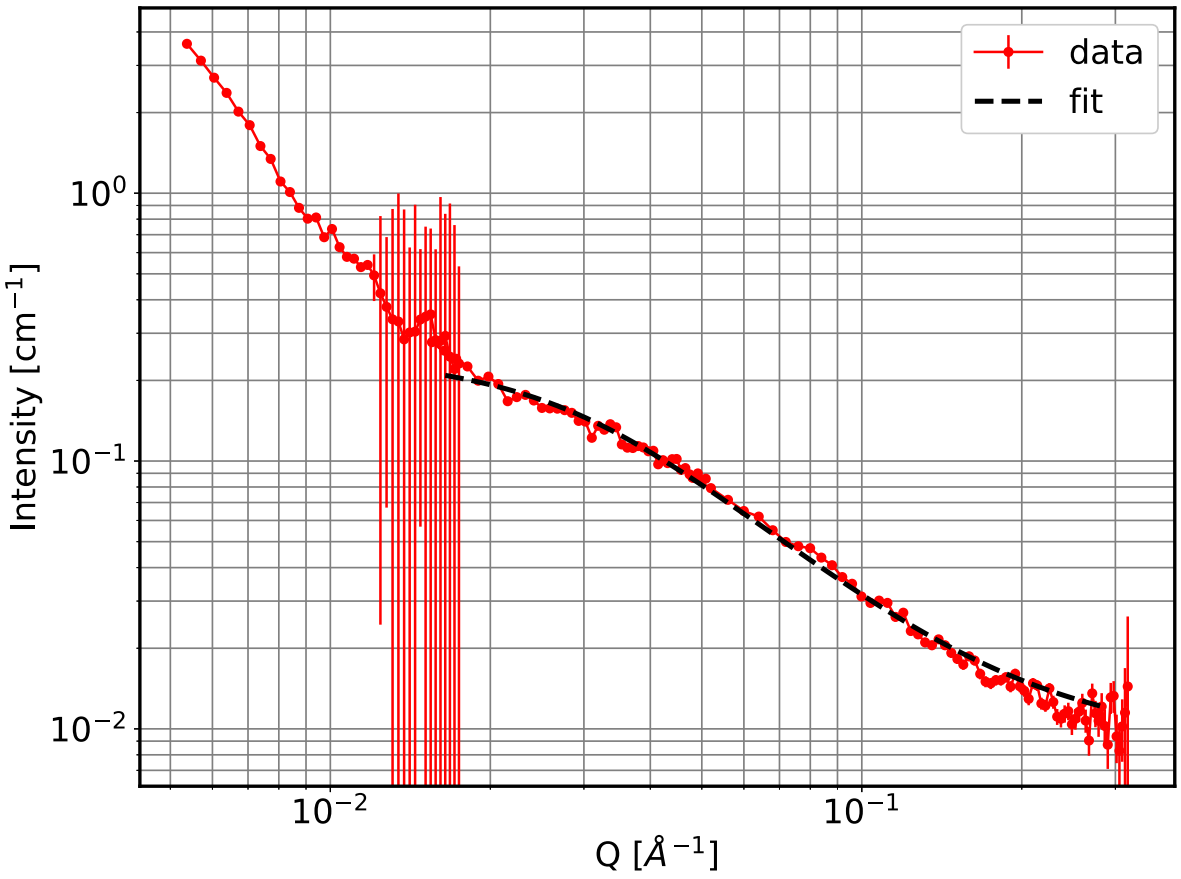


Figure S8: χ^2-values obtained by the different fit models for the A-pBuOzi-A/CUR samples.

Fit Parameter

In the following, the name and the obtained fit parameters of each used Irena model will be given. To take a possible polydispersity of the micelles into account, the core radius was assumed to follow a gaussian distribution function. The presence of such a distribution function will smear out the features at higher Q-values.
Since the experimentally obtained curves are already very smeared and almost featureless, the fitted standard deviations are abnormally high. This smearing is due to a convolution of the real distribution function and a systematical error of every neutron scattering instrument. There are different routines and algorithms in literature, which can take the instrumental smearing into account during fitting[1]. Unfortunately, the used data analysis software did not provide this option. Hence, the obtained standard deviations of the gaussian distribution are systematically higher and cannot be used for polydispersity estimation.

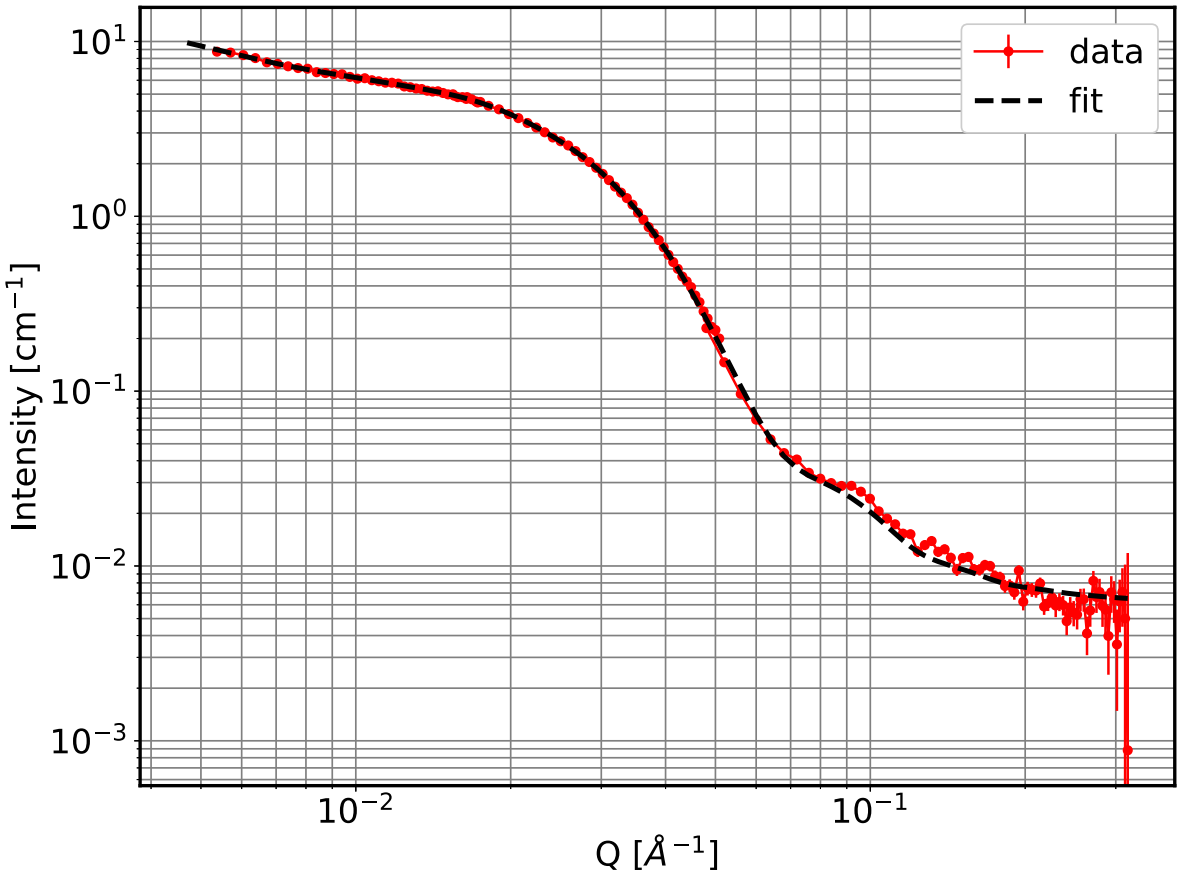
A-pPrOzi-A/CUR: 10/0



simple cylinder form factor

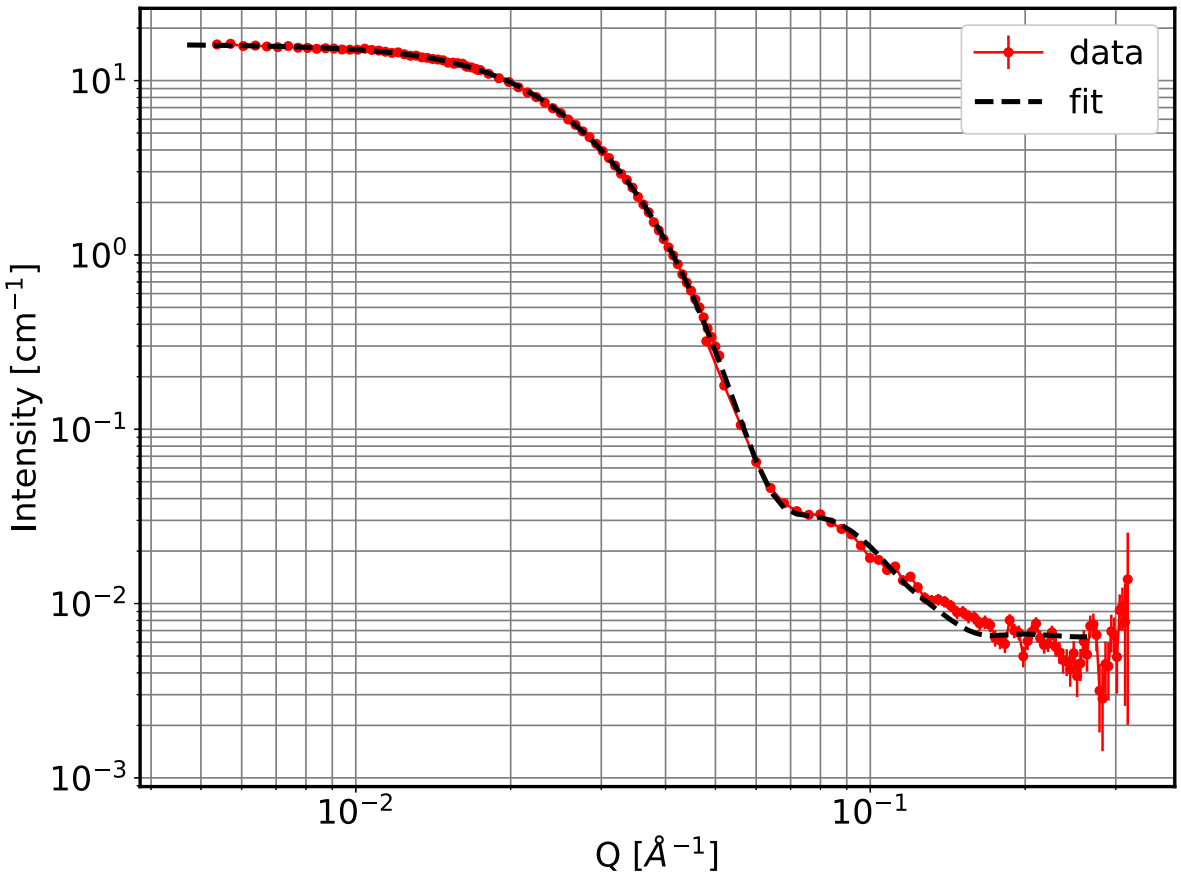
Radius [Å]	12.71 ± 0.61
standard deviation radius [Å]	37.9 ± 1.1
Length [Å]	2.2 ± 0.9
Contrast [10^{20} cm^{-2}]	20.8 ± 1.1
volume fraction	0.00911
Background [cm^{-1}]	0.00899 ± 0.00049

A-pPrOzi-A/CUR: 10/1



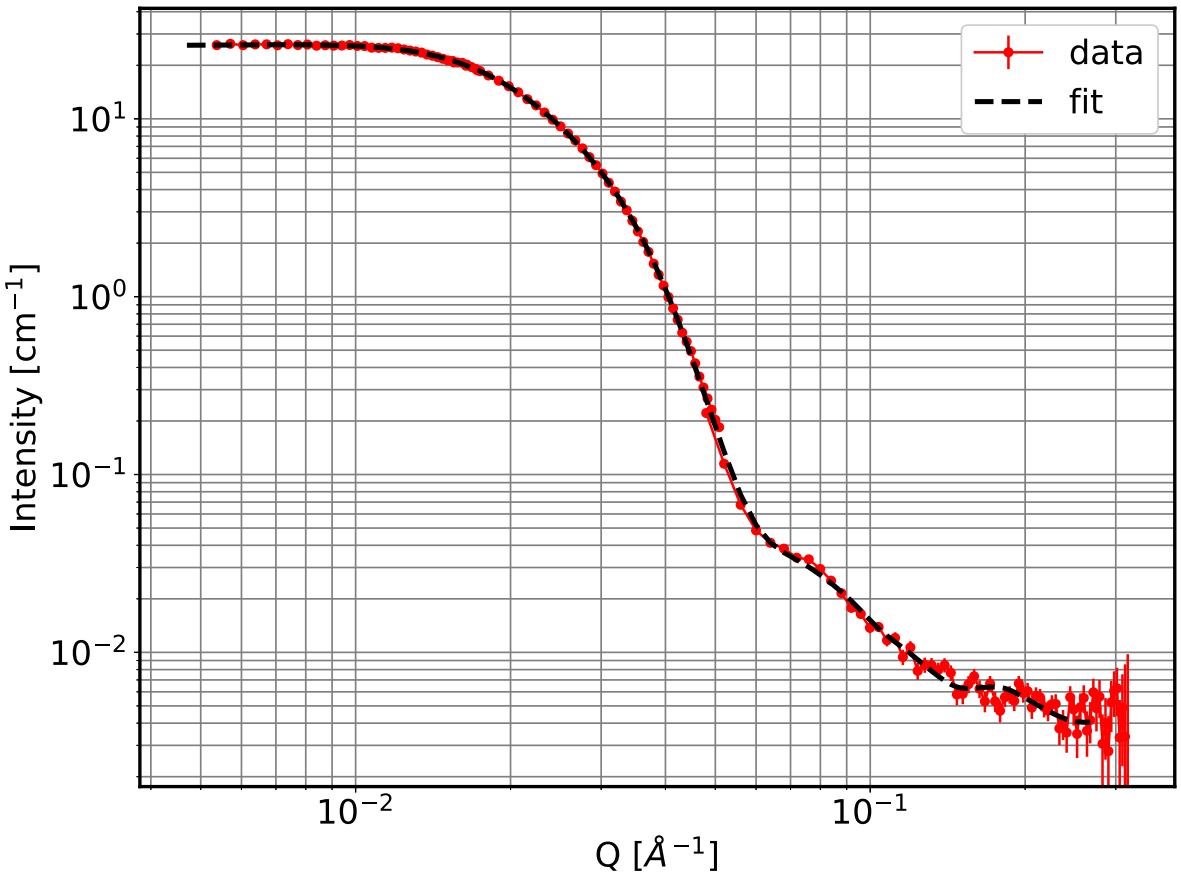
core-shell-shell sphere form factor	
core radius [Å]	8.4 ± 2.1
standard deviation core [Å]	28.02 ± 0.49
Shell thickness 1 [Å]	51.85 ± 0.34
Shell thickness 2 [Å]	9.87 ± 0.44
SLD core [10^{10} cm^{-2}]	3.87 ± 0.13
SLD shell 1 [10^{10} cm^{-2}]	4.14 ± 0.31
SLD shell 2 [10^{10} cm^{-2}]	6.29 ± 0.11
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.00968
Background [cm^{-1}]	0.006078 ± 0.00
hard sphere structure factor	
Correlation length η [Å]	232.0 ± 2.0
Correlation strength κ	0.0120 ± 0.0089

A-pPrOzi-A/CUR: 10/3



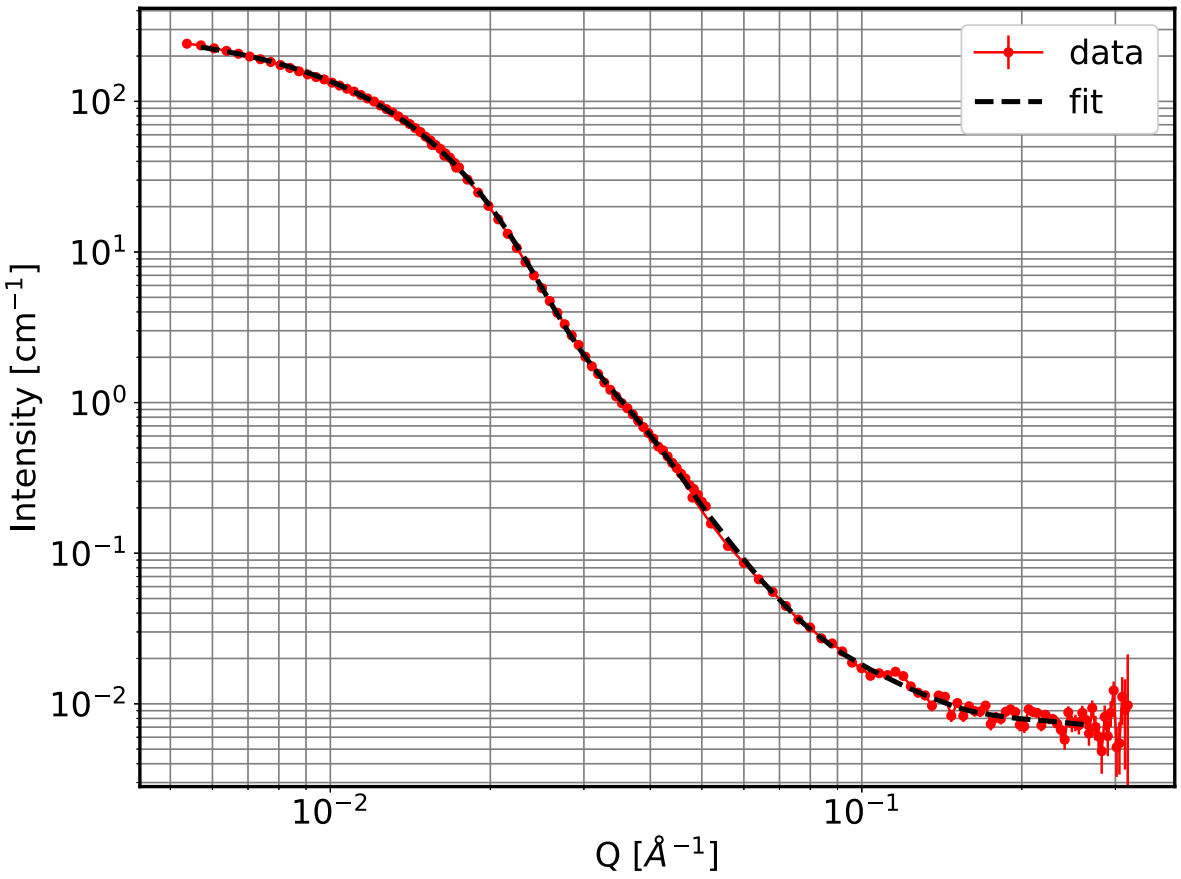
core-shell-shell sphere form factor	
core radius [Å]	10.92 ± 0.97
standard deviation core [Å]	26.17 ± 0.92
Shell thickness 1 [Å]	47.33 ± 0.27
Shell thickness 2 [Å]	13.65 ± 0.44
SLD core [10^{10} cm^{-2}]	1.62 ± 0.28
SLD shell 1 [10^{10} cm^{-2}]	3.580 ± 0.073
SLD shell 2 [10^{10} cm^{-2}]	4.870 ± 0.014
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.01092
Background [cm^{-1}]	0.0046 ± 0.0015
hard sphere structure factor	
Correlation length η [Å]	141.9 ± 5.9
Correlation strength κ	0.028 ± 0.013

A-pPrOzi-A/CUR: 10/5



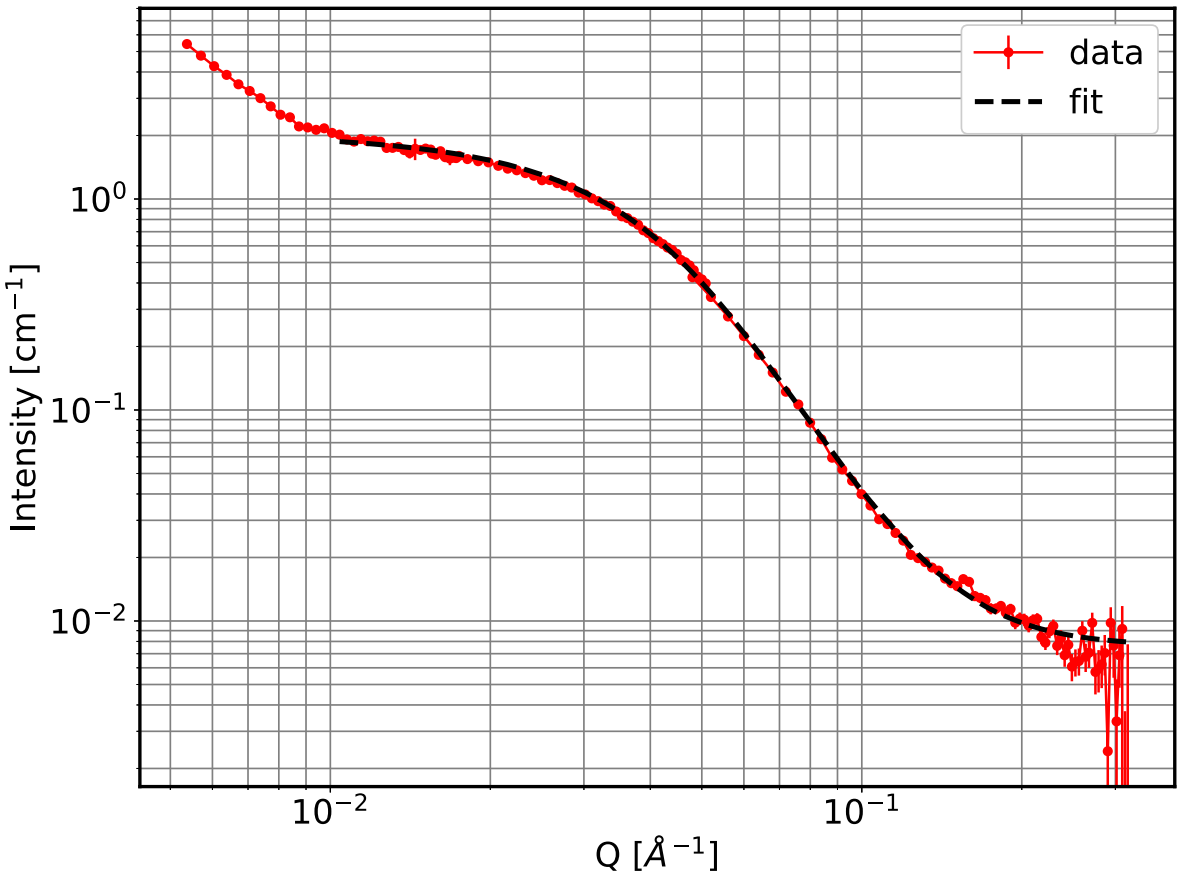
core-shell-shell sphere form factor	
core radius [Å]	25.3 ± 2.8
standard deviation core [Å]	21.68 ± 0.61
Shell thickness 1 [Å]	29.15 ± 3.1
Shell thickness 2 [Å]	33.9 ± 1.1
SLD core [10^{10} cm^{-2}]	1.71 ± 0.27
SLD shell 1 [10^{10} cm^{-2}]	3.110 ± 0.074
SLD shell 2 [10^{10} cm^{-2}]	4.063 ± 0.018
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.01216
Background [cm^{-1}]	0.0047 ± 0.0014
hard sphere structure factor	
Correlation length η [Å]	171.3 ± 5.0
Correlation strength κ	0.036 ± 0.013

A-pPrOzi-A/CUR: 10/10



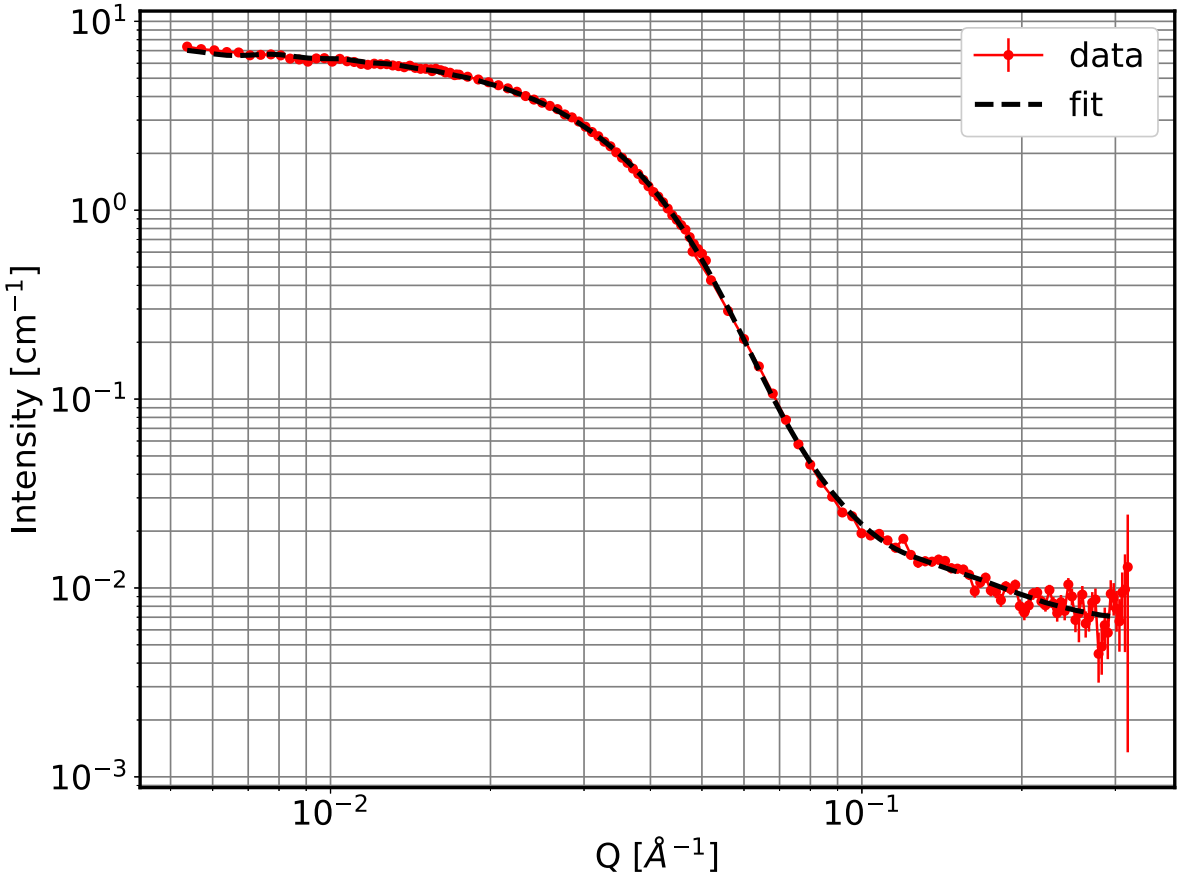
core-shell-shell sphere form factor	
core radius [Å]	110.94 ± 2.3
standard deviation core [Å]	39.57 ± 3.9
Shell thickness 1 [Å]	31.2 ± 1.7
Shell thickness 2 [Å]	52.40 ± 0.89
SLD core [10^{10} cm^{-2}]	1.190 ± 0.068
SLD shell 1 [10^{10} cm^{-2}]	1.970 ± 0.019
SLD shell 2 [10^{10} cm^{-2}]	6.133 ± 0.033
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.01539
Background [cm^{-1}]	0.00702 ± 0.00013
sticky hard sphere structure factor	
Correlation length η [Å]	238.9 ± 5.1
Correlation strength κ	(1.40 ± 0.10)*10^{-6}
Perturbation parameter	0.310 ± 0.011
Stickiness	0.133 ± 0.020

A-pBuOzi-A/CUR: 10/0



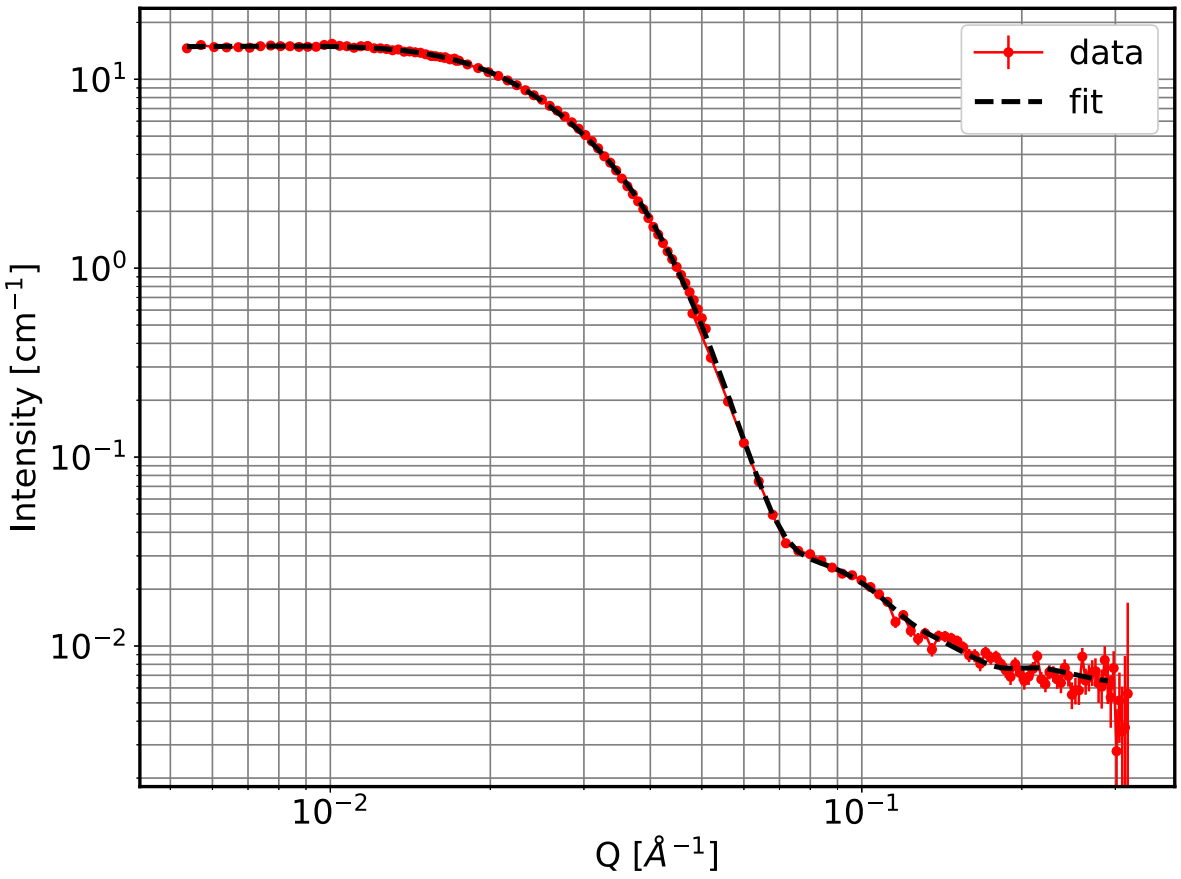
core-shell-shell sphere form factor	
core radius [Å]	15.42 ± 0.68
standard deviation core [Å]	31.6 ± 1.2
Shell thickness 1 [Å]	2.00 ± 0.40
Shell thickness 2 [Å]	1.43 ± 0.18
SLD core [10^{10} cm^{-2}]	3.66 ± 0.27
SLD shell 1 [10^{10} cm^{-2}]	4.10 ± 0.50
SLD shell 2 [10^{10} cm^{-2}]	5.82 ± 0.31
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.00888
Background [cm^{-1}]	0.0076 ± 0.0013
hard sphere structure factor	
Correlation length η [Å]	2093 ± 89
Correlation strength κ	0.469 ± 0.055

A-pBuOzi-A/CUR: 10/1



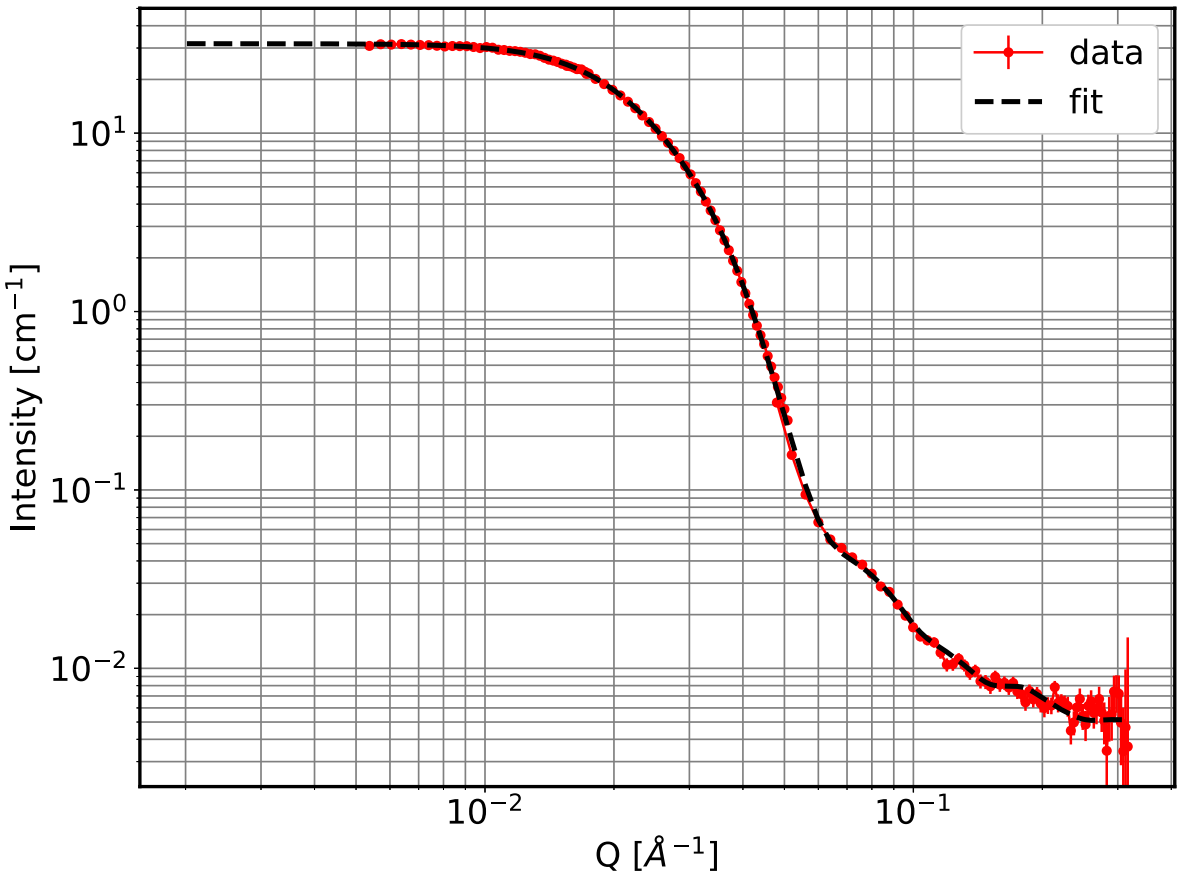
core-shell-shell sphere form factor	
core radius [Å]	28.61 ± 0.65
standard deviation core [Å]	15.9 ± 1.2
Shell thickness 1 [Å]	33.60 ± 0.78
Shell thickness 2 [Å]	2.20 ± 0.28
SLD core [10^{10} cm^{-2}]	3.39 ± 0.34
SLD shell 1 [10^{10} cm^{-2}]	3.89 ± 0.11
SLD shell 2 [10^{10} cm^{-2}]	4.83 ± 0.21
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.00941
Background [cm^{-1}]	0.0079 ± 0.0019
hard sphere structure factor	
Correlation length η [Å]	1195 ± 96
Correlation strength κ	0.142 ± 0.034

A-pBuOzi-A/CUR: 10/3



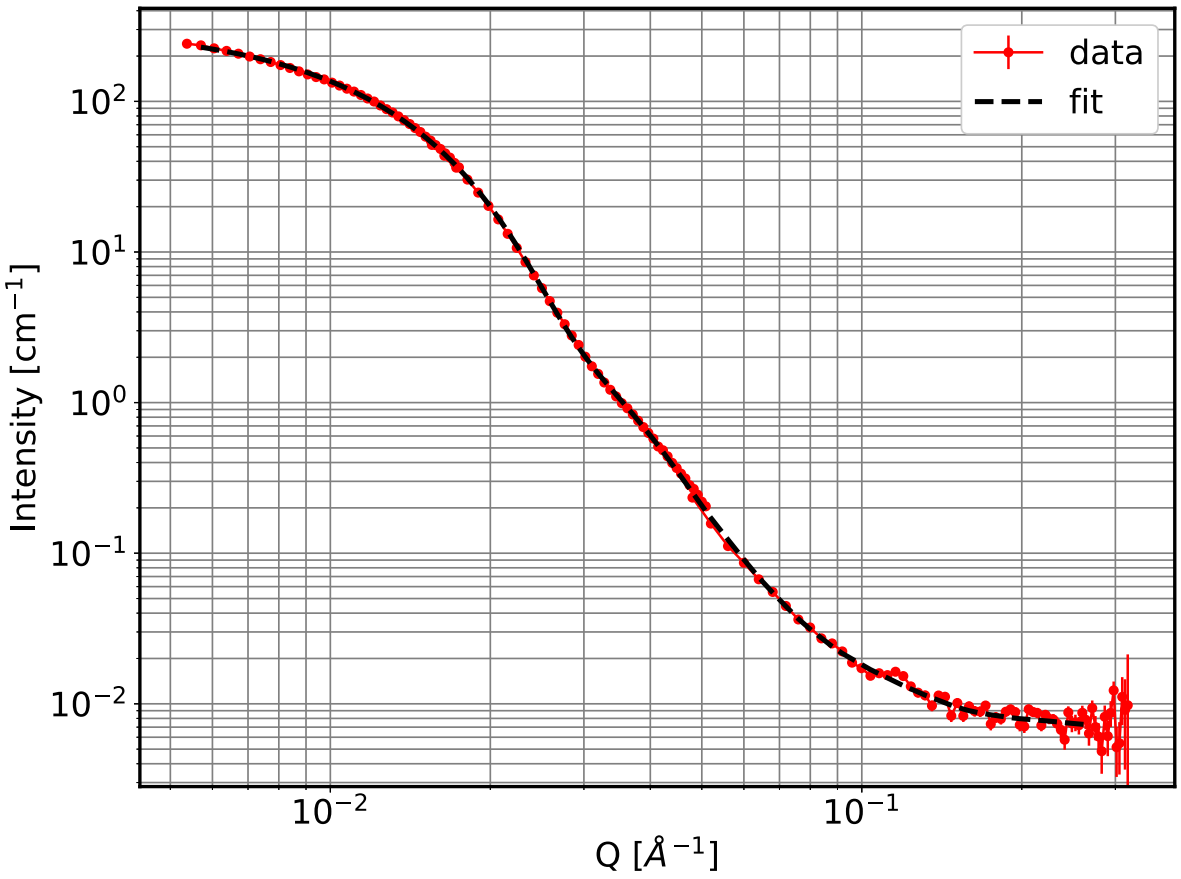
core-shell-shell sphere form factor	
core radius [Å]	14.9 ± 2.6
standard deviation core [Å]	23.2 ± 1.8
Shell thickness 1 [Å]	29.99 ± 0.60
Shell thickness 2 [Å]	29.61 ± 0.79
SLD core [10^{10} cm^{-2}]	1.66 ± 0.64
SLD shell 1 [10^{10} cm^{-2}]	3.00 ± 0.13
SLD shell 2 [10^{10} cm^{-2}]	3.829 ± 0.041
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.01082
Background [cm^{-1}]	0.0063 ± 0.0020
hard sphere structure factor	
Correlation length η [Å]	146.9 ± 5.3
Correlation strength κ	0.30 ± 0.18

A-pBuOzi-A/CUR: 10/5



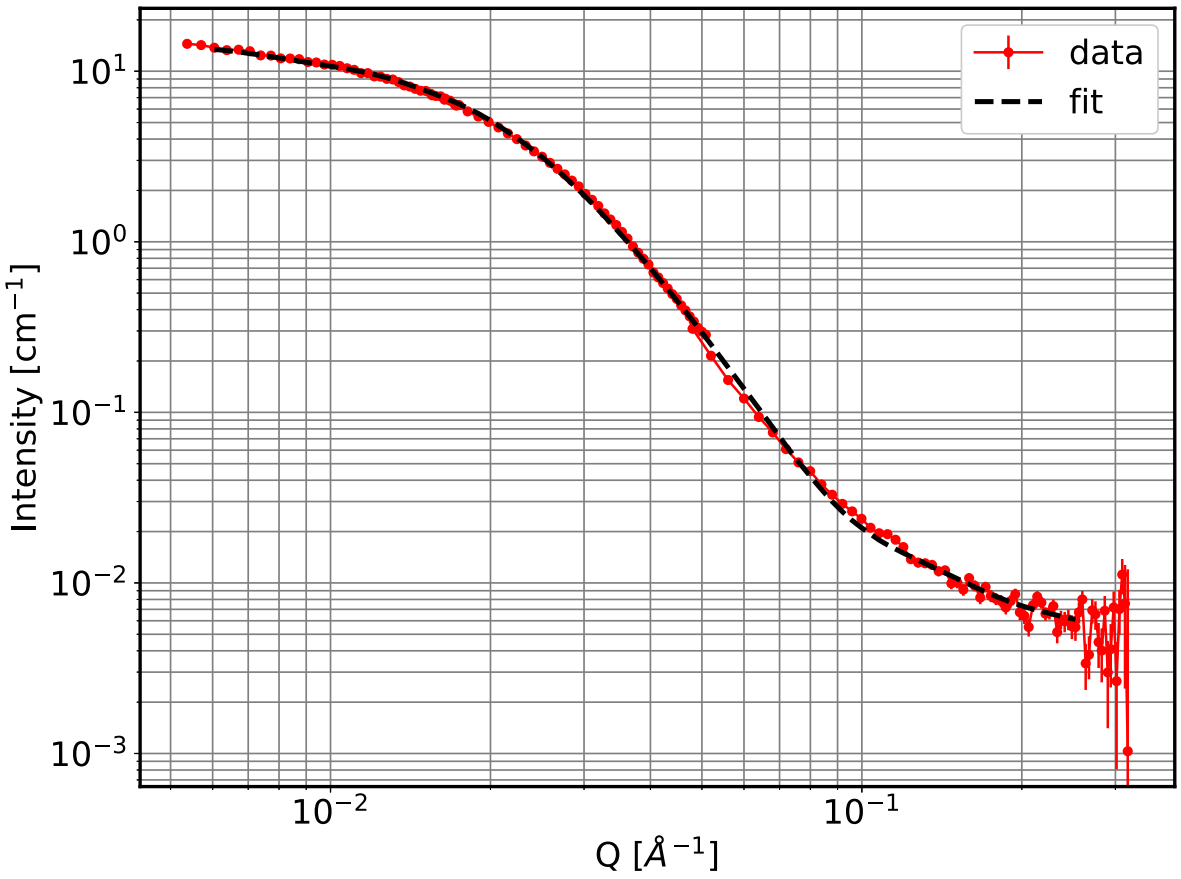
core-shell-shell sphere form factor	
core radius [Å]	19.6 ± 1.0
standard deviation core [Å]	18.91 ± 0.16
Shell thickness 1 [Å]	29.70 ± 0.17
Shell thickness 2 [Å]	33.86 ± 0.43
SLD core [10^{10} cm^{-2}]	1.48 ± 0.27
SLD shell 1 [10^{10} cm^{-2}]	2.770 ± 0.065
SLD shell 2 [10^{10} cm^{-2}]	3.850 ± 0.029
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.01225
Background [cm^{-1}]	0.0052 ± 0.015
hard sphere structure factor	
Correlation length η [Å]	164.1 ± 6.6
Correlation strength κ	0.27 ± 0.15

A-pBuOzi-A/CUR: 10/10



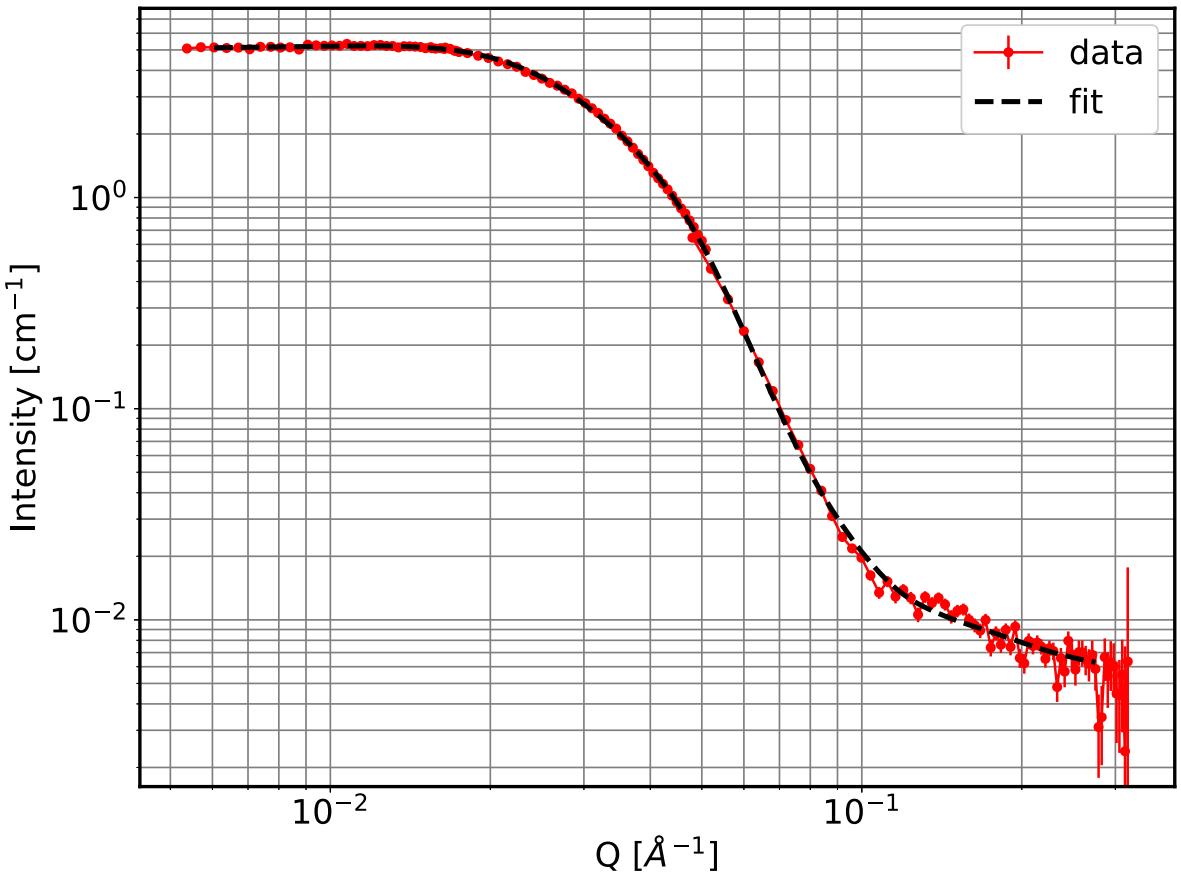
core-shell-shell sphere form factor	
core radius [Å]	19.2 ± 2.2
standard deviation core [Å]	64.9 ± 4.4
Shell thickness 1 [Å]	65.7 ± 1.4
Shell thickness 2 [Å]	40.8 ± 1.2
SLD core [10^{10} cm^{-2}]	2.73 ± 0.14
SLD shell 1 [10^{10} cm^{-2}]	3.060 ± 0.015
SLD shell 2 [10^{10} cm^{-2}]	3.610 ± 0.024
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.01595
Background [cm^{-1}]	0.0049 ± 0.0026
sticky hard sphere structure factor	
Correlation length η [Å]	163.4 ± 5.1
Correlation strength κ	0.00222 ± 0.00088
Perturbation parameter	0.169 ± 0.030
Stickness	0.0323 ± 0.0012

A-pBuOx-A/CUR: 10/0



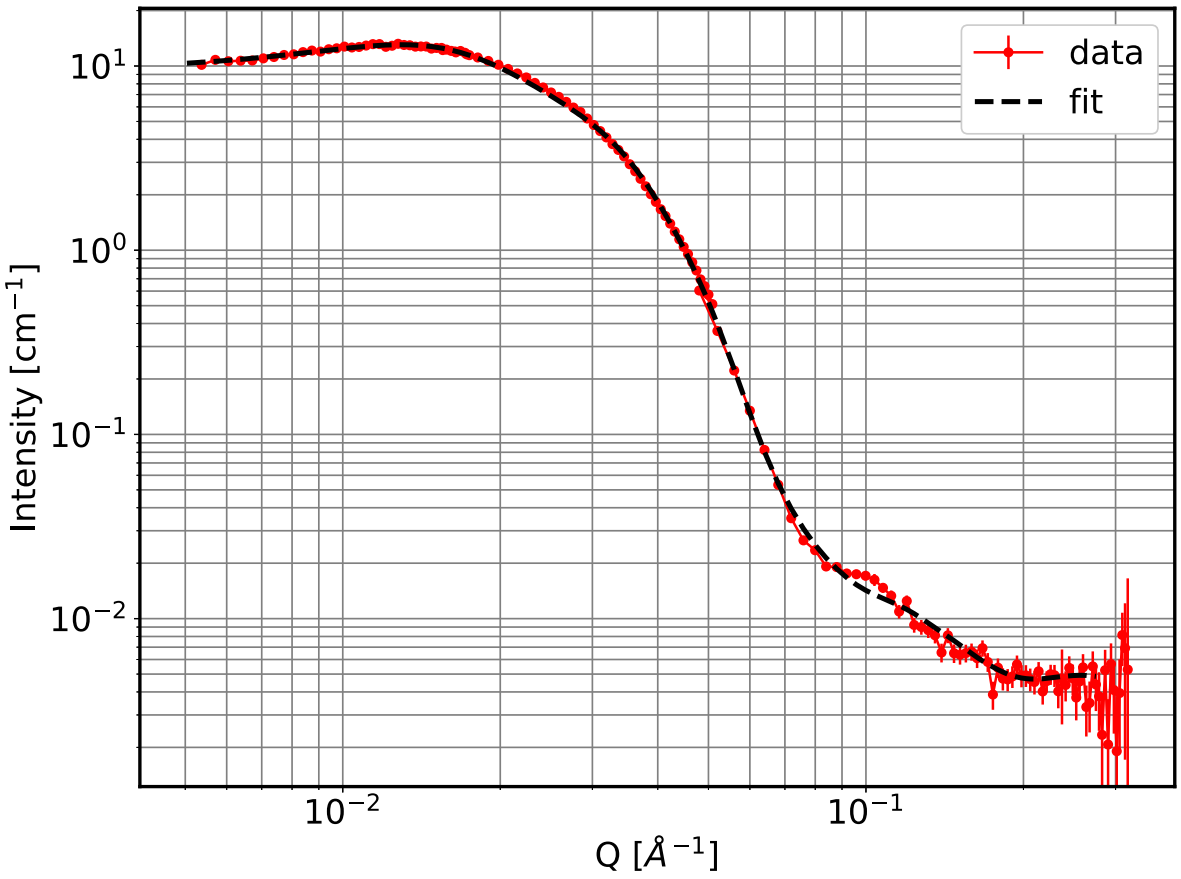
core-shell-shell sphere form factor	
core radius [Å]	45.6 ± 4.1
standard deviation core [Å]	62.5 ± 2.7
Shell thickness 1 [Å]	23.1 ± 1.8
Shell thickness 2 [Å]	3.9 ± 1.2
SLD core [10^{10} cm^{-2}]	3.65 ± 0.37
SLD shell 1 [10^{10} cm^{-2}]	3.87 ± 0.12
SLD shell 2 [10^{10} cm^{-2}]	6.35 ± 0.32
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.0096
Background [cm^{-1}]	0.0058 ± 0.0015
hard sphere structure factor	
Correlation length η [Å]	498.4 ± 8.1
Correlation strength κ	0.116 ± 0.011

A-pBuOx-A/CUR: 10/1



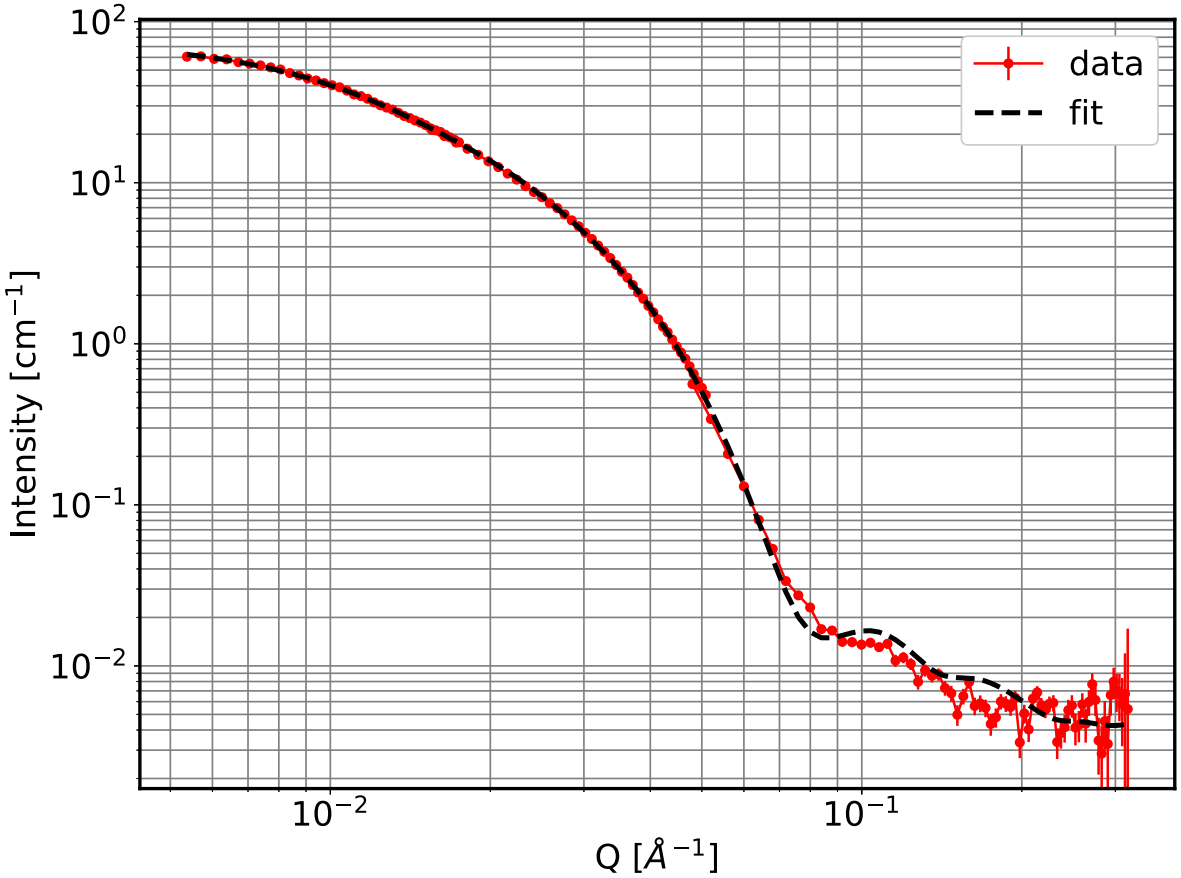
core-shell-shell sphere form factor	
core radius [Å]	29.7 ± 1.9
standard deviation core [Å]	15.35 ± 0.19
Shell thickness 1 [Å]	15.3 ± 2.2
Shell thickness 2 [Å]	13.6 ± 1.1
SLD core [10^{10} cm^{-2}]	3.18 ± 0.22
SLD shell 1 [10^{10} cm^{-2}]	4.05 ± 0.18
SLD shell 2 [10^{10} cm^{-2}]	3.780 ± 0.068
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.00921
Background [cm^{-1}]	0.0058 ± 0.0010
hard sphere structure factor	
Correlation length η [Å]	129.8 ± 3.0
Correlation strength κ	0.353 ± 0.023

A-pBuOx-A/CUR: 10/3



core-shell-shell sphere form factor	
core radius [Å]	28.07 ± 0.92
standard deviation core [Å]	15.7 ± 1.3
Shell thickness 1 [Å]	27.04 ± 0.86
Shell thickness 2 [Å]	18.96 ± 0.51
SLD core [10^{10} cm^{-2}]	1.67 ± 0.42
SLD shell 1 [10^{10} cm^{-2}]	3.310 ± 0.043
SLD shell 2 [10^{10} cm^{-2}]	4.117 ± 0.068
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.00978
Background [cm^{-1}]	0.0043 ± 0.0015
hard sphere structure factor	
Correlation length η [Å]	179.7 ± 2.7
Correlation strength κ	0.693 ± 0.034

A-pBuOx-A/CUR: 10/5



core-shell-shell sphere form factor	
core radius [Å]	1.145 ± 0.042
standard deviation core [Å]	72.8 ± 2.1
Shell thickness 1 [Å]	24.69 ± 0.54
Shell thickness 2 [Å]	16.47 ± 0.62
SLD core [10^{10} cm^{-2}]	0.330 ± 0.027
SLD shell 1 [10^{10} cm^{-2}]	2.91 ± 0.19
SLD shell 2 [10^{10} cm^{-2}]	5.95 ± 0.31
SLD solvent [10^{10} cm^{-2}]	6.39
volume fraction	0.01169
Background [cm^{-1}]	0.0050 ± 0.0016
hard sphere structure factor	
Correlation length η [Å]	143.7 ± 1.2
Correlation strength κ	1.670 ± 0.061

References

[1] J. Pedersen. Resolution effects and analysis of small-angle neutron scattering data. *J. Phys. IV*, **1993**, 03 (C8), 491- 498.