Experimental report

14/10/2020

Proposal: 9-10-1632 **Council:** 10/2019

Title: Self-assembled Nanocapsules as Drug Carriers and Artificial Nano-Enzymes

Research area: Chemistry

This proposal is a new proposal

Main proposer: Alessandro SCARSO

Experimental team: Claudia MONDELLI

Local contacts: Ralf SCHWEINS
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Samples: C51H51Na3O15S3
C66H66Cl3N3O6
C84H120O27

Instrument	Requested days	Allocated days	From	To
D11	2	2	25/08/2020	27/08/2020
D16	6	2	28/08/2020	31/08/2020

Abstract:

New organic nano-capsules from aggregation of triphenylene units with a hydrophobic core (2.0 nm) and a hydrophilic shell (0.7 nm) hold great potentialities as drug carrier for highly hydrophobic drugs like Nitrofurantoin, Naproxen, Vancomycin and anticancer Doxorubicin. The nano-capsules in water allow to bind hydrophobic substrates and to convert them into valuable products like artificial enzymes for bio-tech applications. We prepared three samples with different hydrophilic shells bearing negative or positive charges or hydrophilic PEG units to show a great complementarity of size and distribution to complement different kind of drugs and substrates. A deep understanding of the aggregation properties is fundamental to tailor their cargo ability towards hydrophobic substrates. We ask for 2 days on D11 in order to use its large Q range and fully investigate the size distributions and the shape of aggregates, to further achieve efficient binding for pharmaceutical and bio-technological applications. We ask 6 days on D16 to investigate the effect of the dilution and the different hydrophilic side chains on the shell corresponding to a change of the bond angles of the tails.

ILL RESEARCH PROPOSAL 9-10-1632

Title: **Self-assembled nanocapsules as drug carriers and artificial nano-enzymes**

Proposers: Scarso Alessandro, Mondelli Claudia, Schweins Ralf, Ballester Pablo, Bonifazi Davide.

Beam time: 25/08/2020 – 27/08/2020 D11

28/08/2020 – 27/08/2020 D16

The aim of the experiments was to fully investigate aggregates forming micelle in solutions to further achieve efficient binding for pharmaceutical and bio-technological applications. The engineering of these nano-capsules for highly important industrial applications implies a deep knowledge of the size, the shape and the charge of the artificial nano-carriers. The main goals were to investigate the aggregation number of the organic molecules, the size and distribution of the nano-capsules, the form factor and the details of the local structure of the micelles like superficial charges, size of the apolar core and of the hydrophilic shell: parameters fundamental to study the affinity of the nano-capsules for
different target drugs and substrates.

On D11 we measured 2 systems of triphenylene organic amphiphilic molecules: one with anionic side chains (Tsfan) and an other with neutral side chains (C3PEG) at a wavelength of 4.6 Å and at 3 ditances of the detector: 1.4, 8 an 40 m in order to cover a large Q-range.
The measurements were performed at different concentrations of the system in D_2O in order to avoid the incoherent coming from the solvent, using Helma cells with a thickness of 2 mm.
Tsfan concentrations: 33, 17, 11, 6, 3, 1.6 mM
C3PEG concentrations: 8, 4, 2, 0.75
The lower concentration in both systems it is lower than the respective critical micellar concentration.
Selected curves are reported in figure 1 and 2 respectively.
The data are under analysis using SASView using a core-double shell model.

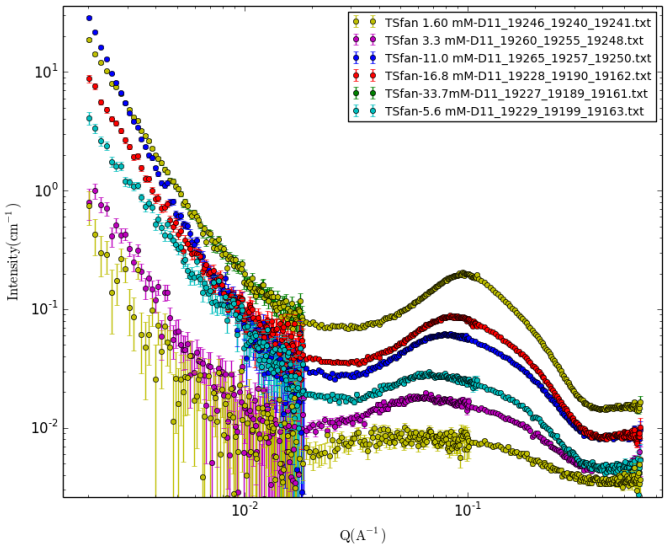

Fig.1 SANS curves at different concentrations for the anionic system called Tsfan

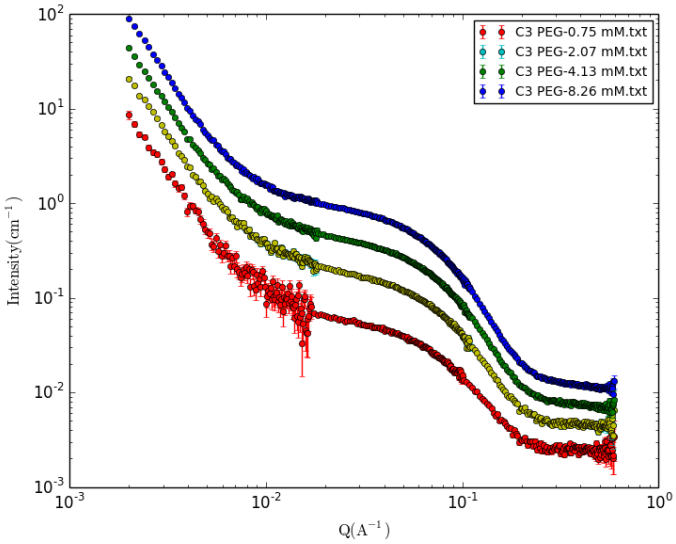

Fig.2 SANS curves at different concentrations for the neutral system called C3PEG

From a preliminary data analysis on the C3PEG it results:
- At 0.75 mM C3 PEG monomers aggregates in micelles and so the c.m.c. are lower than that obtained from the NMR measurements that was estimated to be 1.9mM.
- The "shape" of the signal belong to the presence of the micelles, that goes approximately from 10^{-2} to 10^{-1} Å^{-1}, seems to remain the unvaried for the different curves, indicating that micelles do not change their form factor and thus their shape. Moreover the "peak intensity" that is related to the number of the micelles in the D_2O, increase linearly with the increasing of the concentration of the monomers, see figure.3. This seems indicate that there are not free monomers in the solution and so all of them are involved to form the micelles. Taking into account the 0.75 mM sample's curve, no free monomers seem to be present in solution and the presence of clusters of nano micelles is excluded (that is desirable due to the low concentration of the monomers). The fact the intensity of all the other SANS curves result shifted to higher value linearly with the increasing of the concentration, let us to assume that even for the higher concentrations the presence of clusters is excluded. Due to this fact, the scattering contribution in the low Q region is not attributed to the presence of bigger clusters of nano micelles.
- The slope in log-log plot showed in the low Q region could be due to long term order between the micelles.

We extended the Q range of investigation toward wider angle using D16 to investigate the effect of the dilution and the different hydrophilic side chains on the shell corresponding to a change of the bond angles of the tails and of the first hydration shell
We measured the same samples used on D11 in glass capillars with a diameter of 2 mm in order to optimize the geometry of the sample to the investigate angular range. We performed all measurement at wavelength of 4.49 Å at 3 angular positions of the detector.
We observed a small signal around 4.5 Å^{-1} at a Q value lower than the expected one. Because the low intensity of that signal we had to select only few samples and we had to perform long ancillary measurements (empty can, empty beam, cadmium, vanadium and water for calibration) in order to correct carefully the data (reported in fig 3). The data are under analysis.

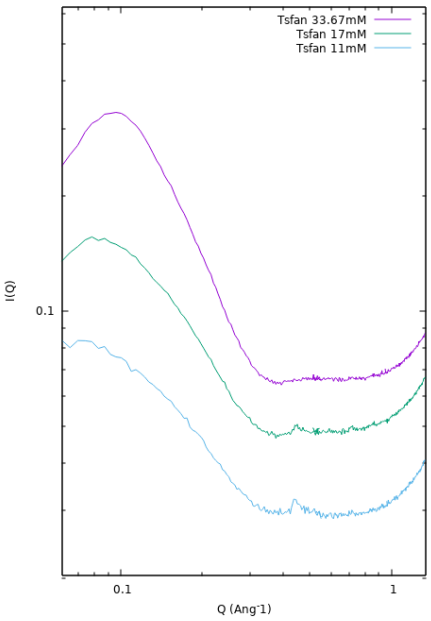

Fig. 3 I(Q) signal for Tsfan at 3 concentrations: 33, 17 and 11 mM.