

## Supporting Information

### Rationalising design of Pluronics-surfactant mixed micelles through molecular simulations and experiments

Divya Patel<sup>a</sup>, Germán Pérez-Sánchez<sup>b</sup>, Miguel Jorge<sup>c</sup>, Debes Ray<sup>d,e</sup>, Vinod K. Aswal<sup>d</sup>, Ketan Kuperkar<sup>a,\*</sup>, João A. P. Coutinho<sup>b</sup>, Pratap Bahadur<sup>f</sup>

<sup>a</sup>Department of Chemistry, Sardar Vallabhbhai National Institute of Technology (SVNIT), Ichchhanath, Surat-395 007, Gujarat, INDIA.

<sup>b</sup>CICECO – Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, Aveiro, 3810-1933, PORTUGAL.

<sup>c</sup>Department of Chemical and Process Engineering, University of Strathclyde, 75 Montrose Street, Glasgow G1 1XJ, UNITED KINGDOM.

<sup>d</sup>Solid State Physics Division, Bhabha Atomic Research Centre (BARC), Trombay, Mumbai, 400 085, Maharashtra, INDIA.

<sup>e</sup>Biomacromolecular systems and processes, Institute of Biological Information Processing, Forschungszentrum Julich- 52428, GERMANY.

<sup>f</sup>Department of Chemistry, Veer Narmad South Gujarat University (VNSGU), Udhana-Magdalla road, Surat-395 007, Gujarat, INDIA.

**\*Corresponding author:** E-mail: [ketankuperkar@gmail.com](mailto:ketankuperkar@gmail.com)

**Declaration of interest:** None

## EXPERIMENTAL

Small-angle neutron scattering experiments were performed at the SANS diffractometer at Guide Tube Laboratory, Dhruva Reactor, Bhabha Atomic Research Centre, Mumbai, India.<sup>1</sup> In SANS, one measures the coherent differential scattering cross-section ( $d\Sigma/d\Omega$ ) per unit volume as a function of wave vector transfer  $Q$  ( $= 4\pi \sin\theta/\lambda$ , where  $\lambda$  is the wavelength of the incident neutrons and  $2\theta$  is the scattering angle). The mean wavelength of the monochromatized beam from neutron velocity selector is 5.2 Å with a spread of  $\Delta\lambda/\lambda \sim 15\%$ . The angular distribution of neutrons scattered by the sample is recorded using a number of 1 m long one-dimensional He<sup>3</sup> position-sensitive detectors (PSDs) in crossed-geometry. The instrument covers a  $Q$ -range of 0.017–0.35 Å<sup>-1</sup>. The data have been analyzed by comparing the scattering from different models to the experimental data. The modelling of the SANS data is described in detail in the next section.

### Small-angle neutron scattering analysis

The differential scattering cross-section per unit volume ( $d\Sigma/d\Omega$ ) as measured for a system of monodisperse particles in a medium can be expressed as

$$\left(\frac{d\Sigma}{d\Omega}\right)(Q) = nV^2(\rho_p - \rho_s)^2 P(Q)S(Q) + B \quad (\text{S1})$$

where  $n$  denotes the number density of particles,  $\rho_p$  and  $\rho_s$  are, respectively, the scattering length densities of particle and solvent and  $V$  is the volume of the particle.<sup>2,3</sup>

$P(Q)$  is the intraparticle structure factor and  $S(Q)$  is the interparticle structure factor.  $B$  is a constant term representing the incoherent background, which is mainly due to the hydrogen present in the sample.

Intraparticle structure factor  $P(Q)$  is decided by the shape and size of the particle and is the square of single-particle form factor  $F(Q)$  as determined by

$$P(Q) = \langle |F(Q)|^2 \rangle \quad (\text{S2})$$

For a spherical particle of radius  $R$ ,  $F(Q)$  is given by<sup>4</sup>

$$F(Q) = 3 \left[ \frac{\sin(QR) - QR \cos(QR)}{(QR)^3} \right] \quad (\text{S3})$$

For a prolate ellipsoidal particle with semi-major and semi-minor axes  $a$  and  $b$ , respectively,

$$F(Q) = \int_0^1 F(Q, \mu) d\mu \quad (\text{S4})$$

where

$$F(Q, \mu) = \frac{3(\sin x - x \cos x)}{x^3} \quad (\text{S5})$$

$$x = Q \left[ a^2 \mu^2 + b^2 (1 - \mu^2) \right]^{1/2} \quad (\text{S6})$$

with

$\mu$  in the above equations refers to the cosine of the angle between the directions of  $a$  and  $Q$ .

For a rod-like micelle of length  $L = 2l$  and cross-sectional radius  $R$ ,

$$P(Q) = \int_0^{\pi/2} \frac{\sin^2(Ql \cos \beta)}{Q^2 l^2 \cos^2 \beta} \frac{4J_1^2(QR \sin \beta)}{Q^2 R^2 \sin^2 \beta} \sin \beta \, d\beta \quad (\text{S7})$$

where  $\beta$  is the angle between the axis of the rod and bisectrix.  $J_1$  is the Bessel function of order unity.<sup>5</sup>

For a system of monodisperse unilamellar vesicles,  $d\Sigma/d\Omega$  can be expressed as

$$\frac{d\Sigma}{d\Omega}(Q, R) = n(\rho_v - \rho_s)^2 \left[ \frac{4}{3} \pi R^3 \frac{3J_1(QR)}{QR} - \frac{4}{3} \pi (R+t)^3 \frac{3J_1[Q(R+t)]}{Q(R+t)} \right]^2 \quad (\text{S8})$$

where  $n$  denotes the number density of the vesicles,  $\rho_v$  and  $\rho_s$  are the scattering length densities of the vesicle bilayer and the solvent, respectively.  $R$  is the radius of the vesicle and  $t$  is the thickness of the bilayer.<sup>6</sup>

$J_1(x)$  is the first order Bessel function and is given by

$$J_1(x) = \frac{\sin x - x \cos x}{x^2} \quad (\text{S9})$$

$S(Q)$  depends on the correlation of the particles and hence interaction between the particles. In general,  $S(Q)$  shows several maxima and minima of decreasing amplitude. The first peak in  $S(Q)$  occurs at  $Q_{\max} \sim 2\pi/d$ , where  $d$  is the average distance between the particles. For an isotropic system,  $S(Q)$  can be written as

$$S(Q) = 1 + 4\pi n \int [g(r) - 1] \frac{\sin Qr}{Qr} r^2 dr \quad (\text{S10})$$

where  $g(r)$  is the radial distribution function. It is the probability of finding another particle at a distance  $r$  from a reference particle centered at the origin.<sup>7</sup> The details of  $g(r)$  depend on the interaction potential  $U(r)$  between the particles. Thus, one has to have the knowledge of  $U(r)$  for calculating  $S(Q)$ . This in turn implies that the measured  $S(Q)$  can be used to obtain information about the interaction potential  $U(r)$ .

Here,  $S(Q)$  has been calculated using the mean spherical approximation developed by Hayter and Penfold<sup>4,8</sup>. In this approximation, the particle (in this case, *micelle*) is treated as a rigid equivalent sphere of diameter  $d$  interacting with another micelle through a screened Coulomb potential  $u(r)$  given by the relation:

$$u(r) = u_0 d \exp[-\kappa(r-d)] / r, \quad r > d \quad (\text{S11})$$

Where  $u_0$  is the potential at  $r = d$  and the Debye-Huckel inverse screening length  $\kappa$  is evaluated by using the expression

$$\kappa = \left( \frac{8\pi N_A e^2 I}{10^3 \varepsilon k_B T} \right)^{1/2} \quad (\text{S12})$$

Where  $N_A$ ,  $e$ ,  $I$ ,  $\varepsilon$ ,  $k_B$  and  $T$  denote Avogadro number, electronic charge, ionic strength of the micellar solution, dielectric constant of the solvent solution, Boltzmann constant, and absolute temperature, respectively.

The contact potential  $u_0$  is given by

$$u_0 = \frac{Z^2 e^2}{\pi \varepsilon \varepsilon_0 \sigma (2 + \kappa \sigma)^2} \quad (\text{S13})$$

where  $\varepsilon_0$  is the permittivity of free space.

Fractional charge is calculated as  $\alpha = Z/N_{\text{agg}}$ , where  $Z$  is the effective micellar charge.

The polydispersity in the size distribution of particles is incorporated using the following integration

$$\frac{d\Sigma}{d\Omega}(Q) = \int \frac{d\Sigma}{d\Omega}(Q, R) f(R) dR + B \quad (\text{S14})$$

where  $f(R)$  is the size distribution of the vesicles and usually accounted by a log-normal distribution as given by

$$f(R) = \frac{1}{\sqrt{2\pi} R \sigma} \exp \left[ -\frac{1}{2\sigma^2} \left( \ln \frac{R}{R_{\text{med}}} \right)^2 \right] \quad (\text{S15})$$

where  $R_{\text{med}}$  is the median value and  $\sigma$  is the standard deviation (polydispersity) of the distribution.<sup>7</sup> The mean radius ( $R_m$ ) is given by  $R_m = R_{\text{med}} \exp(\sigma^2/2)$ .

The data have been analyzed by comparing the scattering from different models to the experimental data and selecting the model that provided the best fit to the data. Throughout the data analysis, corrections were made for instrumental smearing, where the calculated scattering profiles were smeared by the appropriate resolution function to compare with the measured data<sup>9</sup>. The radius for spherical micelles, semi-major and semi-minor axes for ellipsoidal micelles, and cross-sectional radius and length for the rod-like micelles have been used as fitting parameters, and their analysed values are listed in the corresponding Tables. The scattering length densities of the core, shell, solvent and background have also been fitted. The fitted parameters in the analysis were optimized using a nonlinear least-squares fitting program to the model scattering.

The aggregation number ( $N_{\text{agg}}$ ) from SANS measurements has been calculated by using the following relationship:

$$N_{\text{agg}} = V_{\text{m}}/V_{\text{PPO}} \quad (\text{S16})$$

where  $V_{\text{m}}$  is the micellar volume and is given by  $V_{\text{m}} = 4\pi R^3/3$  with  $R$  is the core radius of spherical micelles. For ellipsoidal micelles,  $V_{\text{m}} = 4\pi ab^2/3$  where  $a$  and  $b$  are semi-major and semi-minor axes, respectively.  $V_{\text{PPO}}$  is the molecular volume of the hydrophobic tail of the block copolymer and is calculated using the formula:

$$V_{\text{PPO}} = (n \times 96.3) \text{ \AA}^3 \quad (\text{S17})$$

where the volume of a single PO unit is 96.3  $\text{\AA}^3$  and  $n$  is the number of PO blocks in that particular block copolymer. In case of mixed micelles, it represents the hydrophobic part of the mixture and is given by:

$$V_{\text{h}} = V_{\text{h}}^1 + C_2/C_1 V_{\text{h}}^2 \quad (\text{S18})$$

where  $V_{\text{h}}^1$  and  $V_{\text{h}}^2$  are the molecular volumes of hydrophobic part of the micelle and additive, respectively.  $C_1$  and  $C_2$  are the concentrations of the micelle and additive, respectively.

#### References:

1. Aswal, V.; Goyal, P. Small-angle neutron scattering diffractometer at Dhruva reactor. *Curr. Sci.* **2000**, 7(79) 947-953.
2. Hayter J.; Penfold J. Determination of micelle structure and charge by neutron small-angle scattering. *Colloid Polym Sci.* **1983**, 261, 1022–1030.
3. Ray, D.; Aswal, V.; Kohlbrecher, J. Synthesis and Characterization of High Concentration Block Copolymer-Mediated Gold Nanoparticles. *Langmuir* **2011**, 27, 7, 4048–4056.
4. Hayter, J.; Penfold, J. Self-consistent structural and dynamic study of concentrated micelle solutions. *J. Chem. Soc., Faraday Trans.* **1981**, 1(77), 1851-1863.
5. Sikder, A.; Ray, D.; Aswal, V.; Ghosh, S. Hydrogen-Bonding-Regulated Supramolecular Nanostructures and Impact on Multivalent Binding.
6. Sikder, A.; Ray, D.; Aswal, V.; Ghosh, S. Hydrogen Bonding Regulated Supramolecular Nanostructures and Impact on Multivalent Binding. *Angew. Chem.* **2019**, 131(6), 1620-1625.
7. Ashcroft, N.; Lekner, J. Structure and Resistivity of Liquid Metals. *Phys. Rev.* **1966**, 145, 83 –90.

8. Pedersen J. Analysis of small-angle scattering data from colloids and polymer solutions: modeling and least-squares fitting. *Adv. Colloid Interface Sci.* **1997**, 70, 171-210.
9. Bevington, P. Data Reduction and Error Analysis for Physical Sciences. *McGraw-Hill, New York, 1969*.

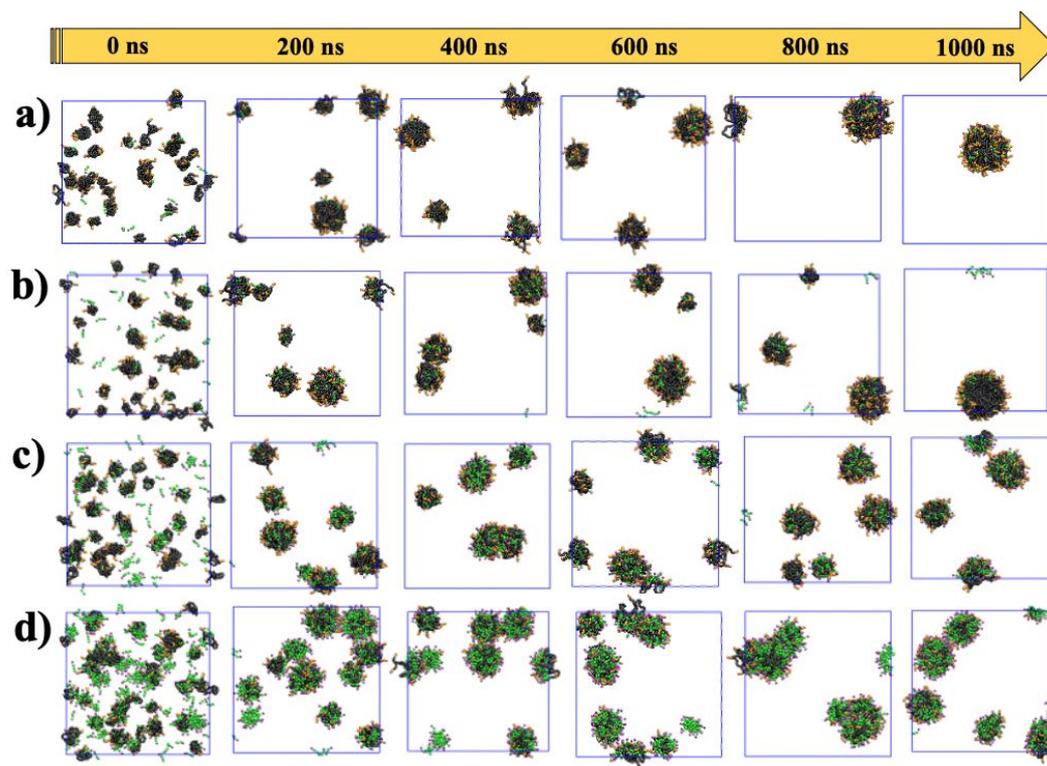
## METHODOLOGY

### *Coarse-grained molecular model*

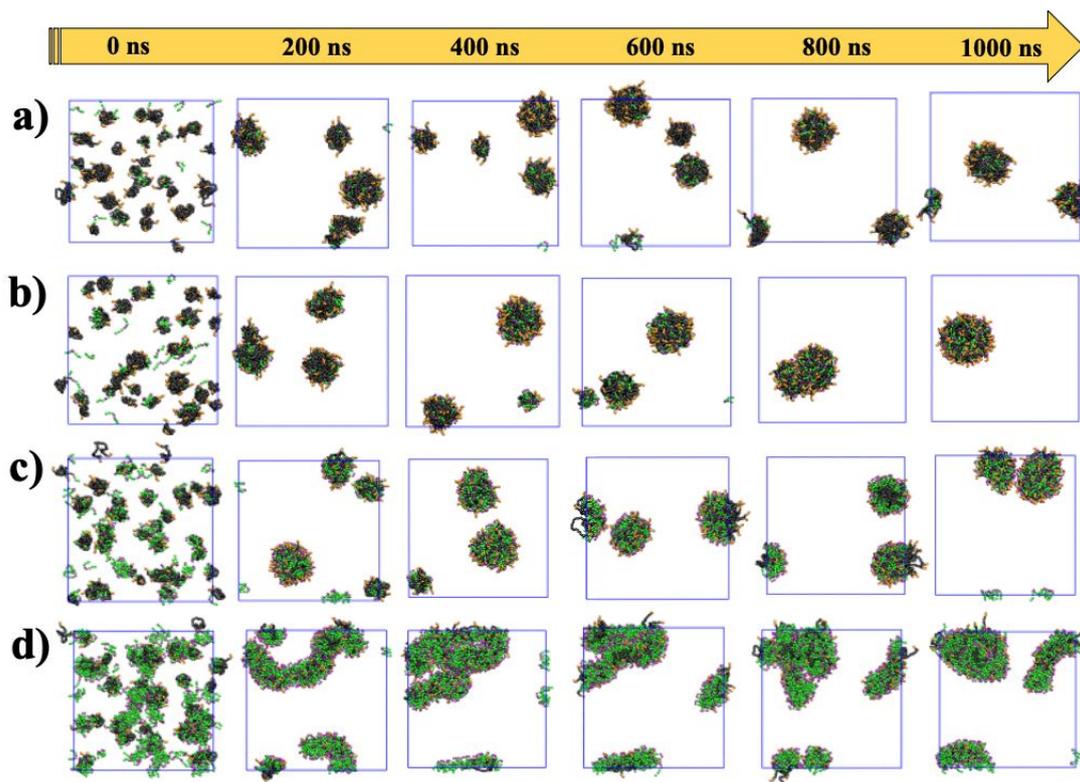
**Table S1.** Details of the CG-MD simulations carried out in this work.

<b>Simulation</b>	<b>Systems</b>	<b>L81</b>	<b>Surfactant</b>	<b>W</b>
run1	L81/W	50	0	190000
run2	DTAB/W	0	240	90000
run3	DDAB/W	0	500	370000
run4	12-2-12/W	0	500	530000
run5	L81/W	50	0	62000
run6	L81/5 mM DTAB/W	50	25	62000
run7	L81/1 0mM DTAB/W	50	50	62000
run8	L81/30 mM DTAB/W	50	152	62000
run9	L81/90 mM DTAB/W	50	455	62000
run10	L81/5 mM 12-2-12/W	50	25	62000
run11	L81/10 mM 12-2-12/W	50	50	62000
run12	L81/30 mM 12-2-12/W	50	152	62000
run13	L81/90 mM 12-2-12/W	50	455	62000
run14	L81/5 mM DDAB/W	50	25	62000
run15	L81/10 mM DDAB/W	50	50	62000
run16	L81/30 mM DDAB/W	50	152	62000
run17	L81/90 mM DDAB/W	50	455	62000

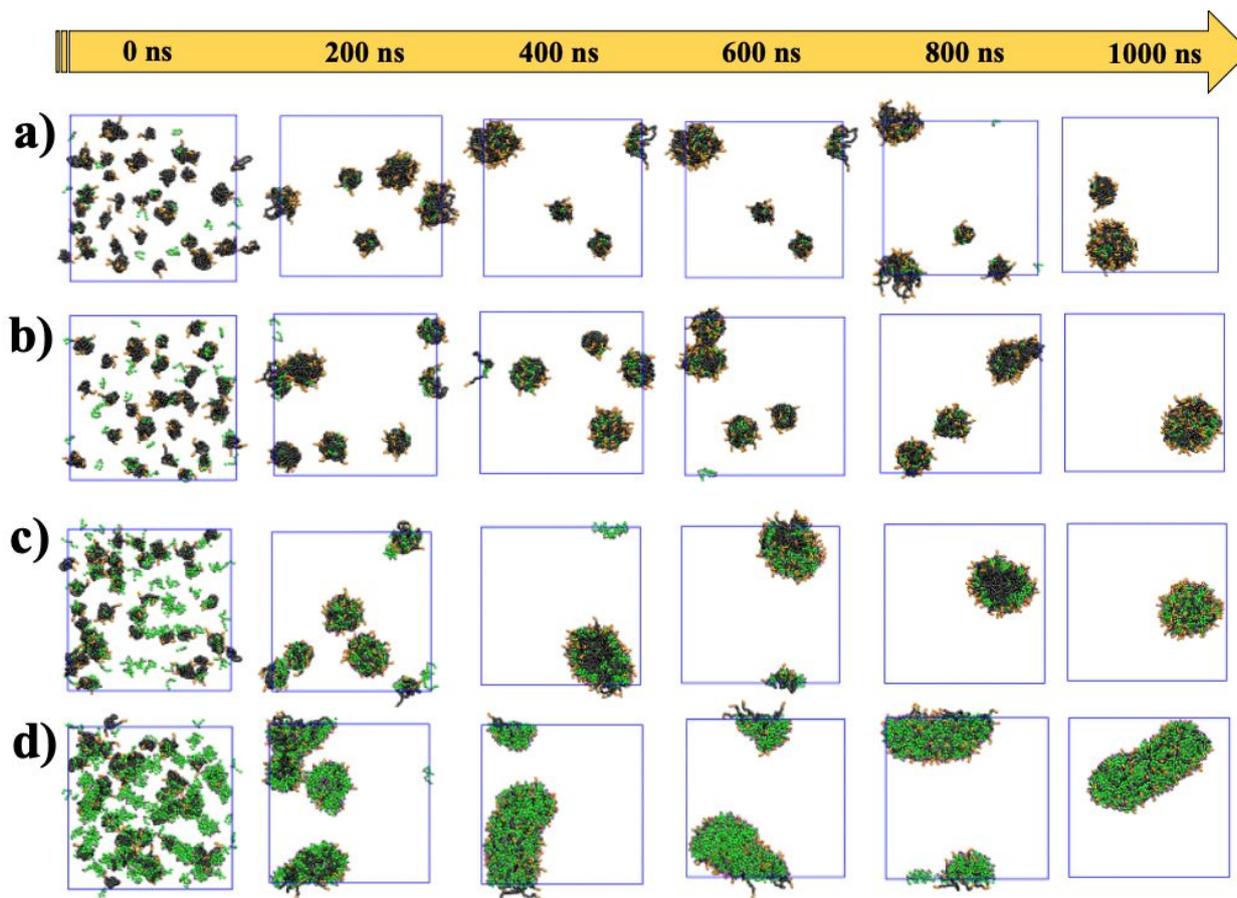
## RESULTS AND DISCUSSION



**Figure S1.** CG-MD simulation snapshots at different stages for the 3 %w/v L-81 aqueous solution mixed with a) 5mM, b) 10mM, c) 30mM and d) 90mM DTAB concentrations. The colour code is the same as in **Figure 11** and water molecules and bromide counterions were removed for clarity.



**Figure S2.** CG-MD simulation snapshots at different stages for the 3 %w/v L-81 aqueous solution mixed with a) 5mM, b) 10mM, c) 30mM and d) 90mM Gemini 12-2-12 concentrations. The colour code is the same as in **Figure 12** and water molecules and bromide counterions were removed for clarity.



**Figure S3.** CG-MD simulation snapshots at different stages for the 3 %w/v L-81 aqueous solution mixed with a) 5mM, b) 10mM, c) 30mM and d) 90mM DDAB concentrations. The colour code is the same as in **Figure 13** and water molecules and bromide counterions were removed for clarity.