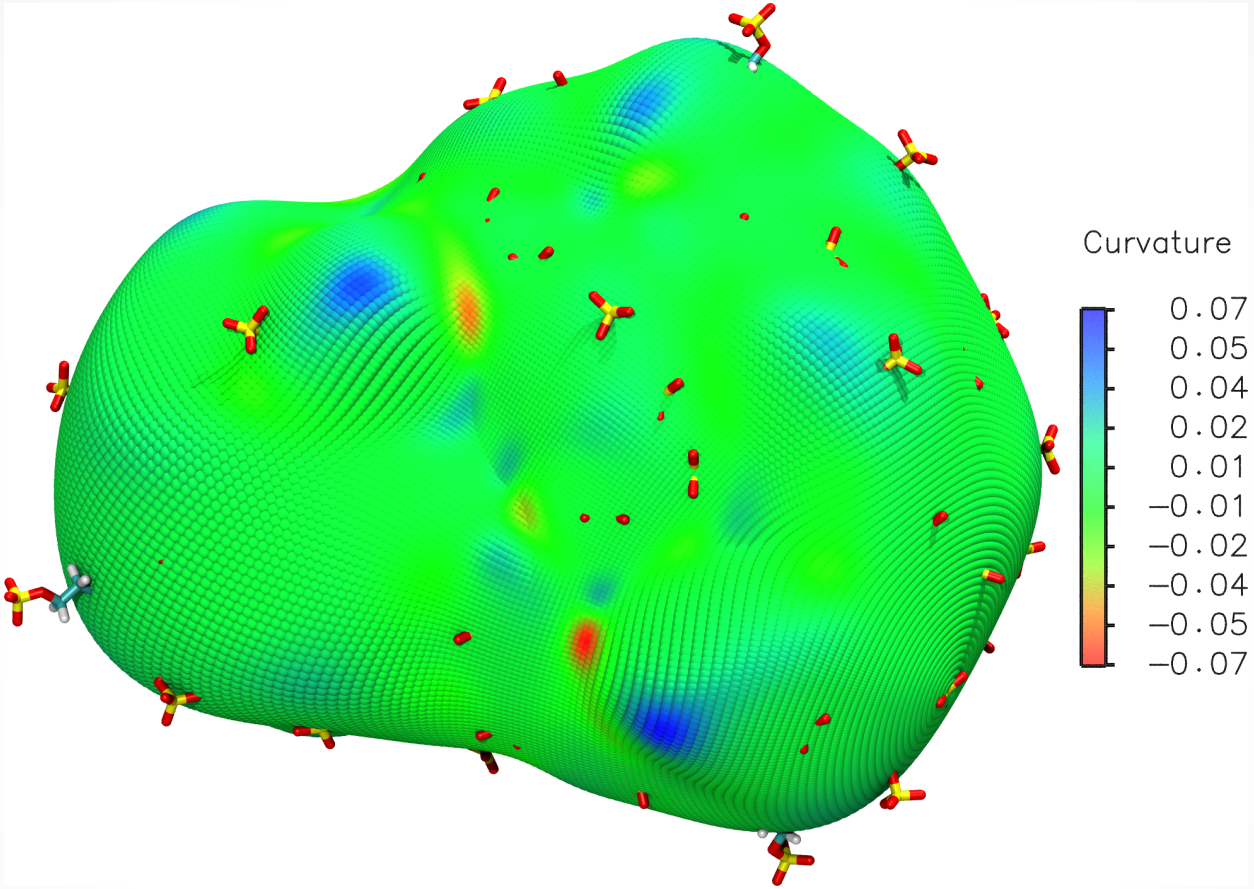
HPC & SASSIE modelling of detergent micelles

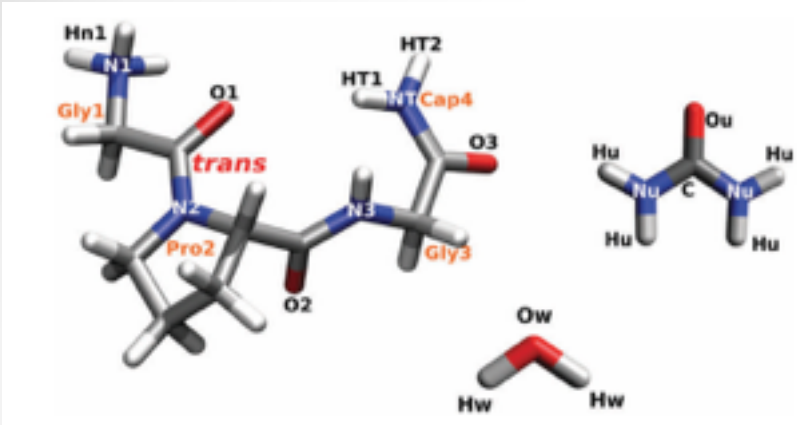


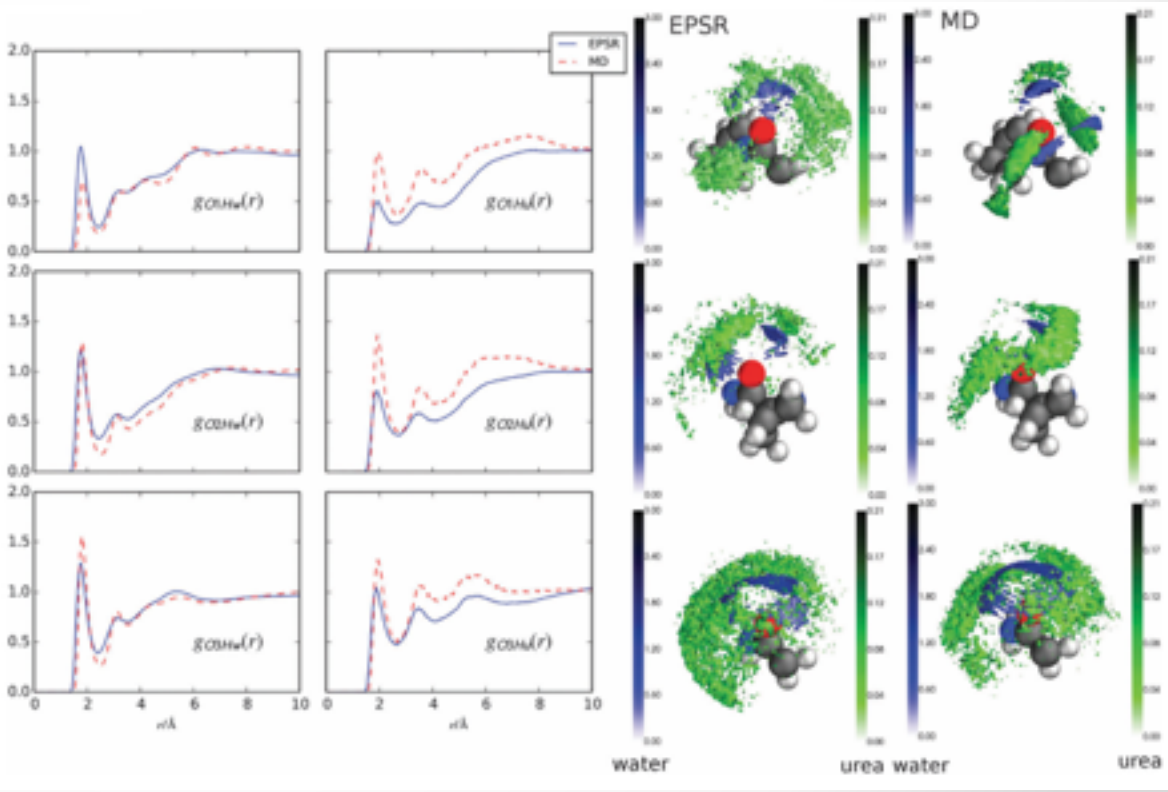
Chris Lorenz
Biophysics & Soft Matter Group
Theory & Simulation of Condensed Matter Group
Physics Department
King's College London

KING'S College LONDON

CANES

Large q comparison to neutrons





Dan Allen – PhD student
Self-assembly of soft matter
Drug encapsulation

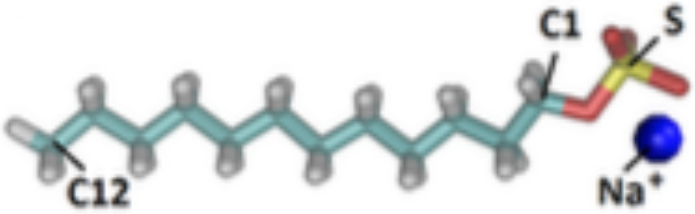
Prof. Jayne Lawrence, Dr. David Barlow & Yussif Saaka (KCL IPS): Neutron scattering & other biophysical experimental techniques

Introduction

- Self-assembly of soft nanomaterials proves to be very challenging for molecular simulations
  - Time scale of self-assembly is on the order of 10^{-4} s
  - Typical concentrations of experimental interest are on the order of 10^{-5} – 10^{-3} M, with aggregate sizes on the order of 100 molecules
  - Properties of interest for micelles are often concentration dependent
  - Therefore in explicit solvent systems that results in systems on the order of 10^{5}-10^{7} atoms

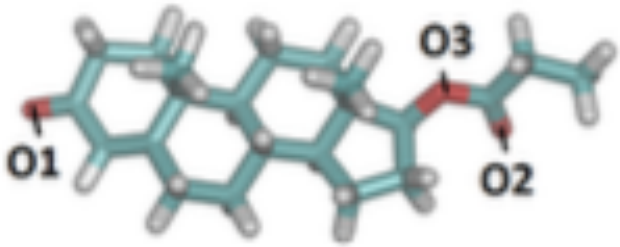
Background

- Sodium dodecyl sulfate (SDS) is a commonly used surfactant in the pharmaceutical industry as a wetting and solubilising agent.
  - Antimalarial drug (Krishna et al. *J. Pharm. Sci.* **78**, 574-576 (1989))
  - Ibuprofen (Rangel-Yagui et al. *J. Pharm. Sci.* **41**, 237-246 (1996))
  - Anti-cancer drug (Enache et al. *Int. J. Pharm.* **390**, 100-106 (2010))



Background

- Testosterone propionate
  - Steroid used in hormone replacement therapy
  - Little is known regarding interactions with solubilising agents
  - Contains both **hydrophilic** (O1, O2 & O3) and **hydrophobic** regions which makes it difficult to predict where it will reside within micelle



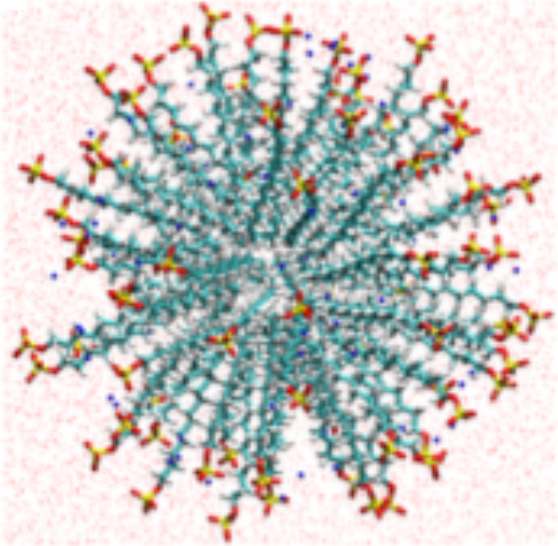
Simulation set-up

Pre-assembled SDS micelle with 80 molecules

CHARMM forcefield w/ TIP3P for water

Concentration of SDS is 3 g/mol (same as exp't.)

Allen et al. *J. Phys. Chem. B* **118**, 13192-13201 (2014)



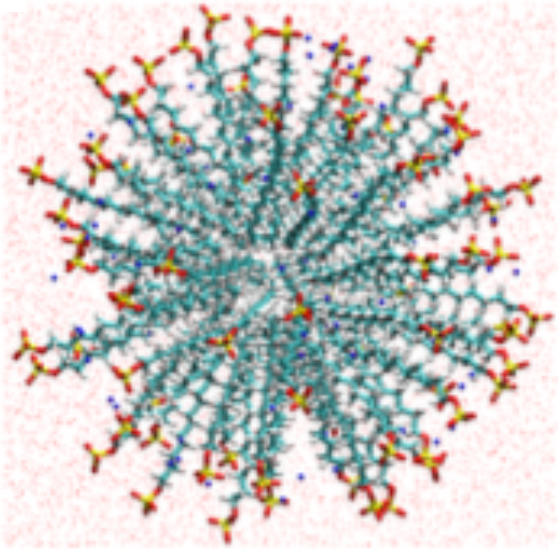
Simulation set-up

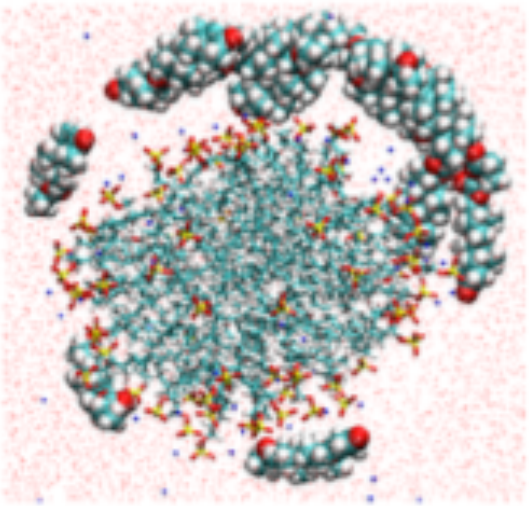
Pre-assembled SDS micelle with 80 molecules

Equilibrated SDS micelle (76 molecules) before surrounding with 13 TSTP molecules

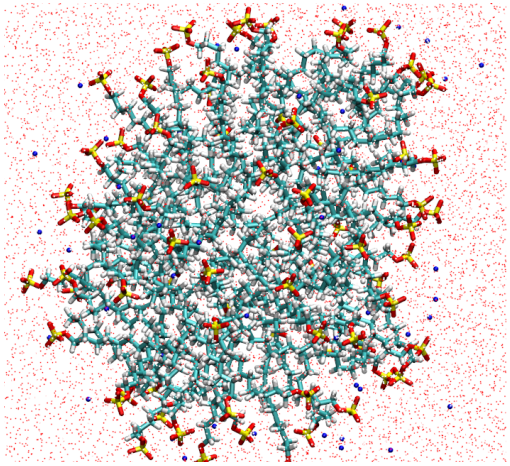
CHARMM forcefield w/ TIP3P for water

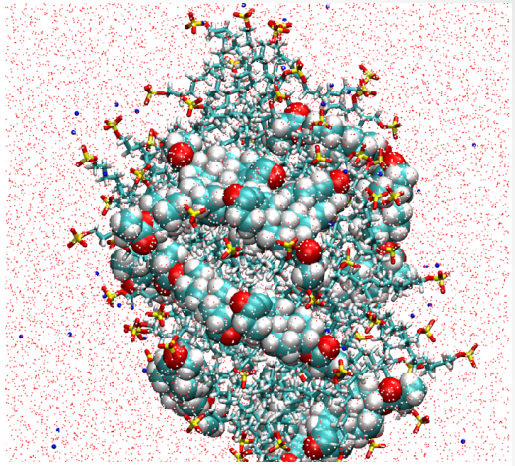
Concentration of SDS is 3 g/mol (same as exp't.)





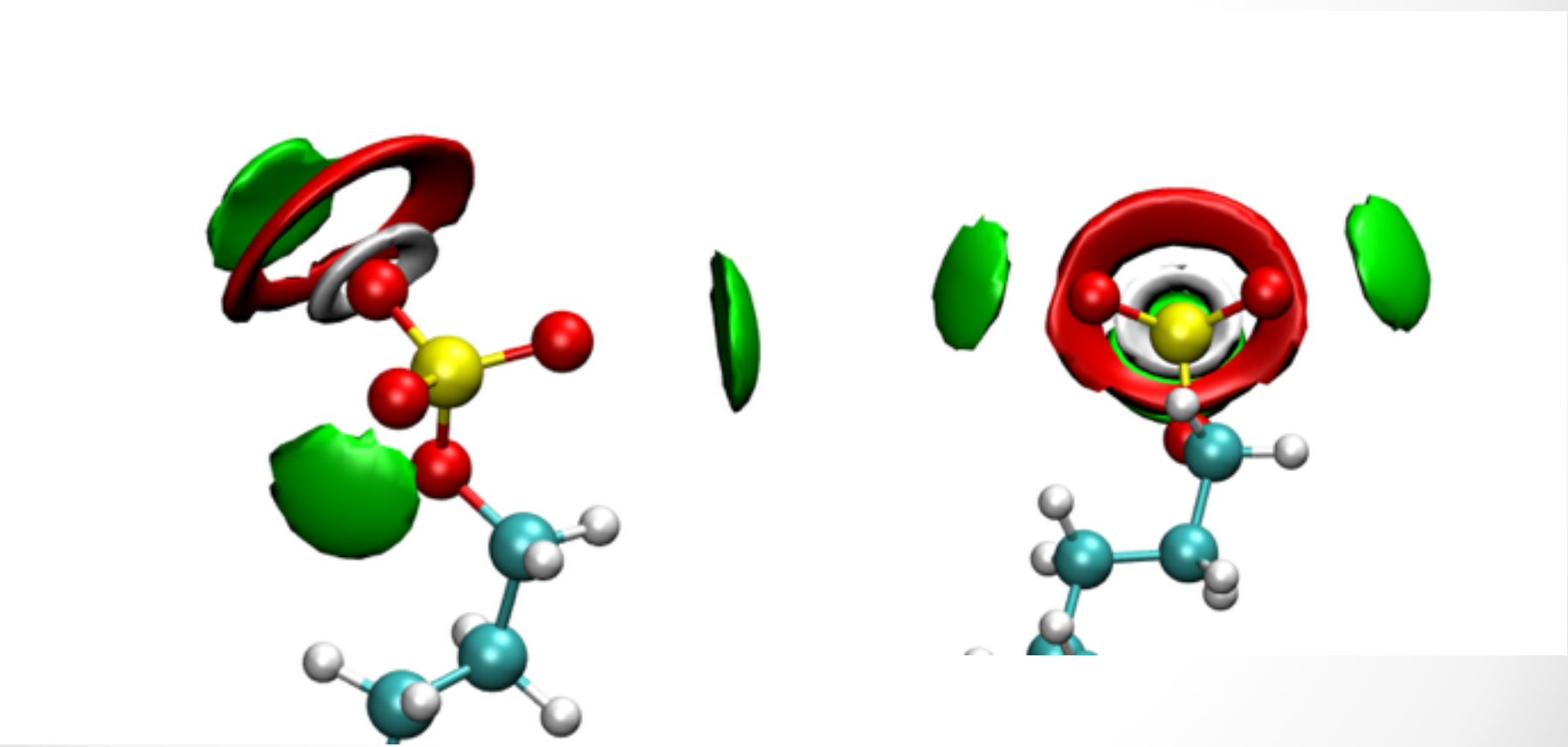
Resulting aggregates



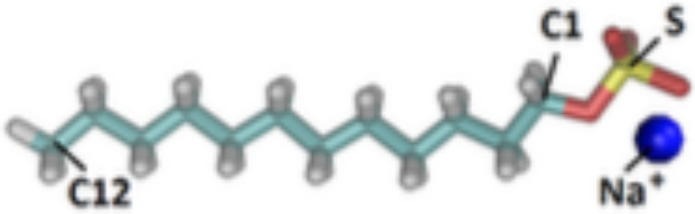


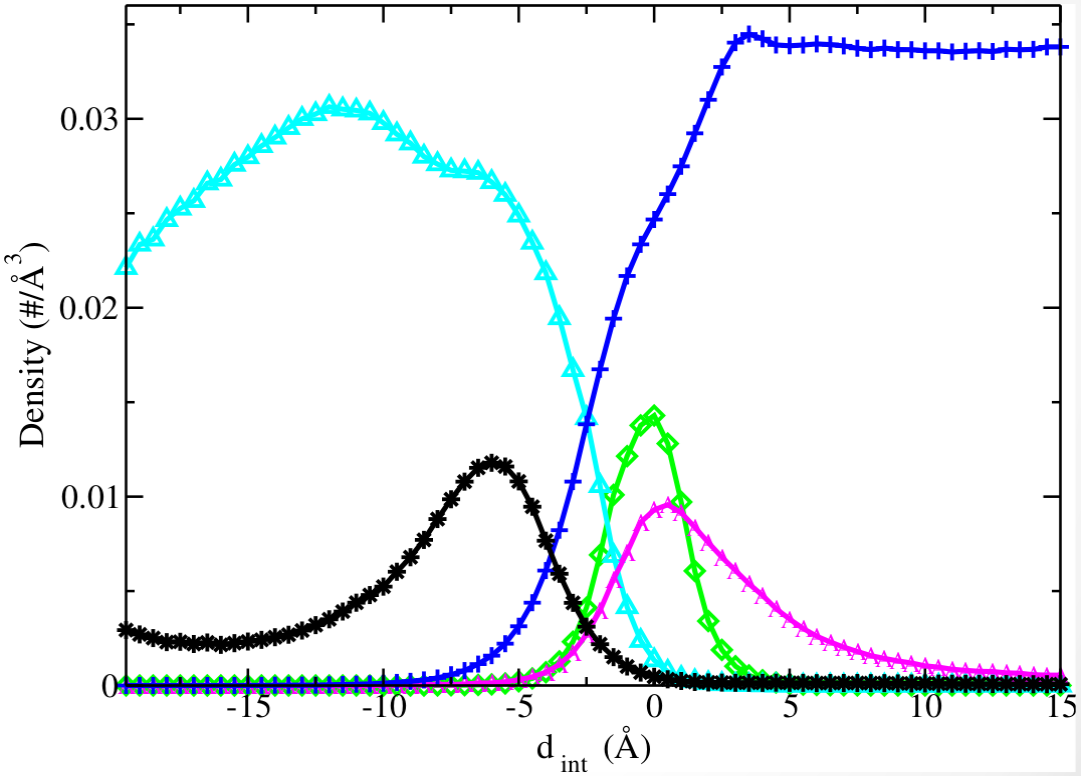
	Blank SDS micelle	SDS micelle with TSTP
Eccentricity	0.11 ± 0.07	0.16 ± 0.08
I_x/I_y	1.01 ± 0.17	1.03 ± 0.18
I_x/I_z	1.04 ± 0.20	1.18 ± 0.29
I_y/I_z	1.04 ± 0.18	1.15 ± 0.28
Max l_x (Å)	48.06 ± 4.98	48.22 ± 5.81
Max l_y (Å)	48.21 ± 4.37	49.75 ± 5.67
Max l_z (Å)	49.18 ± 5.01	53.15 ± 6.06
SASA/molecule (Å^2)	169.9 ± 4.5	156.1 ± 4.2
Total SASA (Å^2)	13592.8 ± 358.2	13734.9 ± 371.6
Voronoi Surface Area/molecule (Å^2)	149.7 ± 2.6	136.9 ± 2.2
Total Voronoi Surface Area (Å^2)	11972.1 ± 206.6	12181.2 ± 193.5

Where are ions & water located?



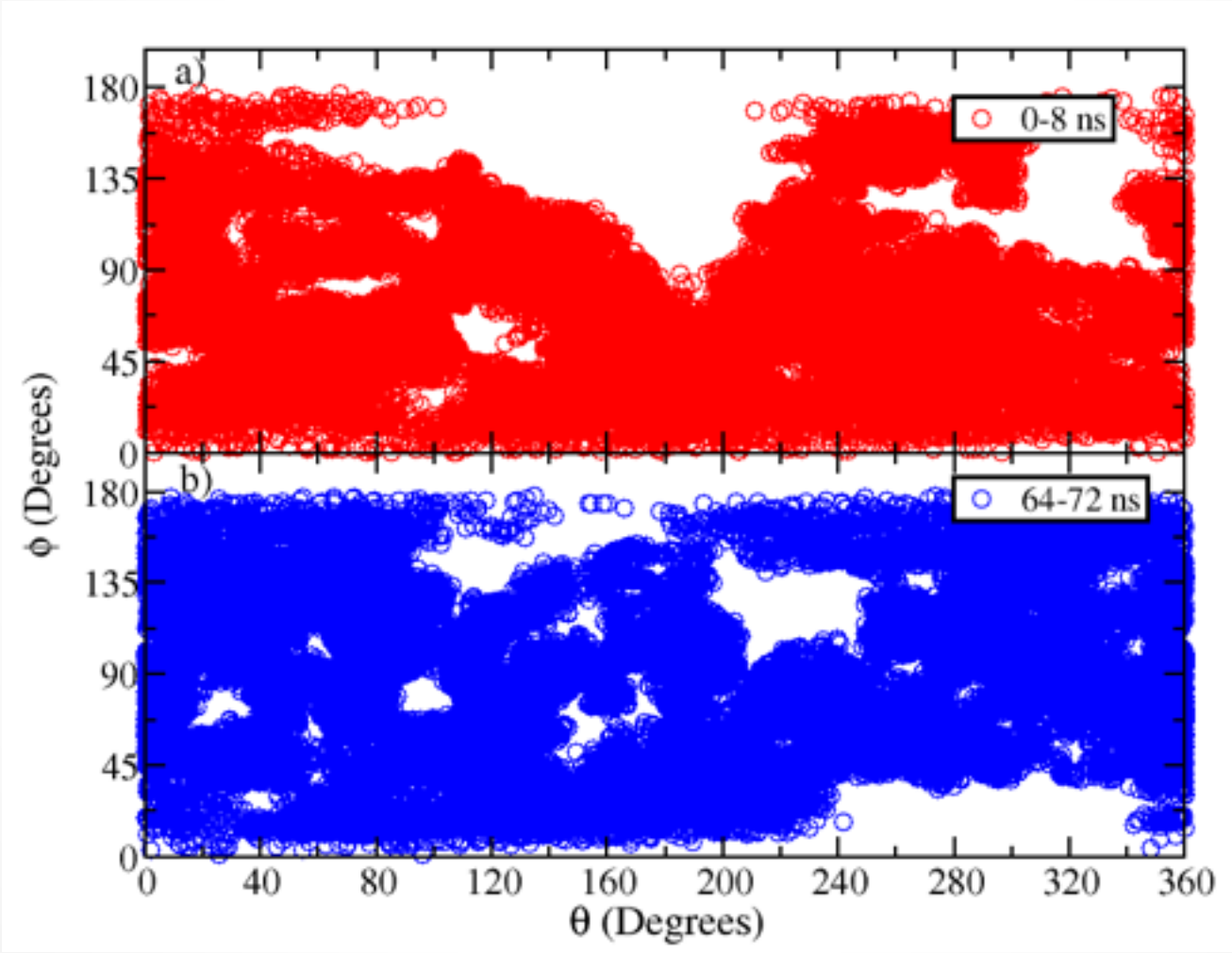
Where is drug located?





Found drug was just under head group — useful for fitting neutron data

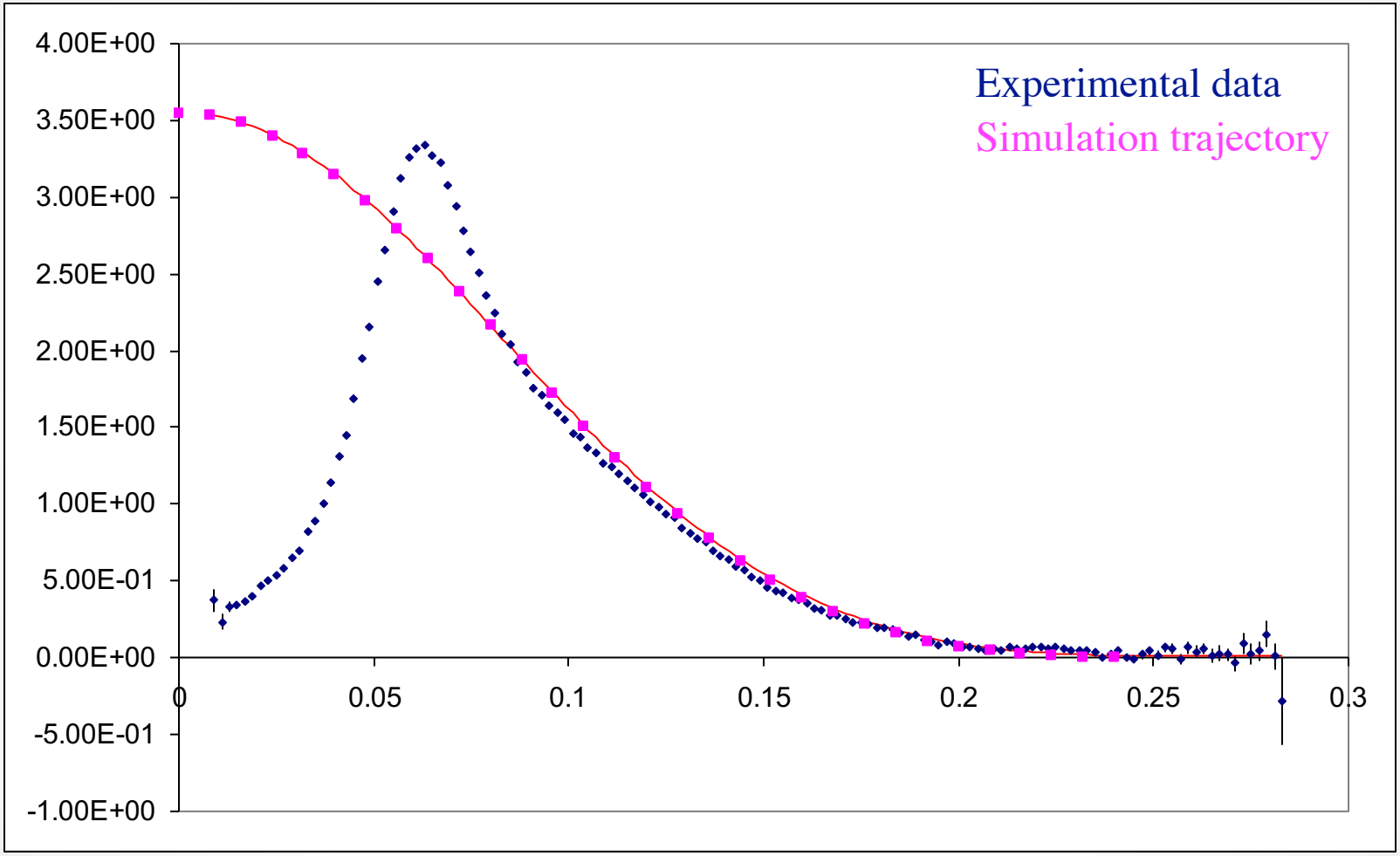
Drug moves on surface



Application of SASSIE

- Tried to use SASSIE to generate SANS profile from simulated structure of SDS micelle
- Read in CHARMM topology file for SDS
- Converted LAMMPS trajectory to dcd files
- Used all-atom SAScalc (beta version)

Application of SASSIE



At large Q the SANS profiles agree well

At small Q, not so much … repulsive behaviour between micelles is not modelled by SASSIE

Further thoughts

- Simulations need aggregation number from experiment.
- Simulations can provide lots of relevant structural properties that can be used to gain molecular scale understanding of micelles and also help to fit neutron scattering data
- Still some way to go to be able to directly compare SANS and MD data

EPSRC
Engineering and Physical Sciences Research Council