UiO : Universitetet i Oslo

bio3 chemical life sciences

How Styrene Maleic Acid Copolymers Induce Membrane Fracture and Disc Formation

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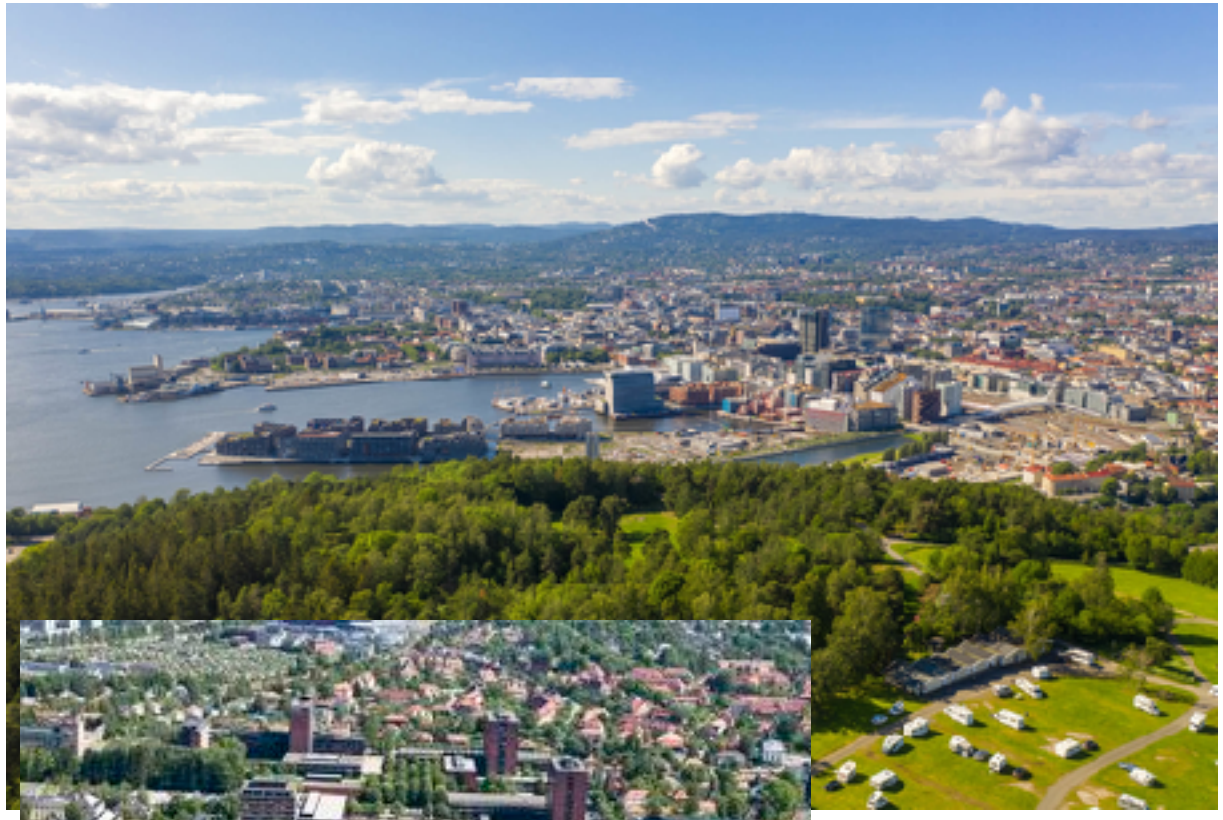
Soft matter group in Oslo



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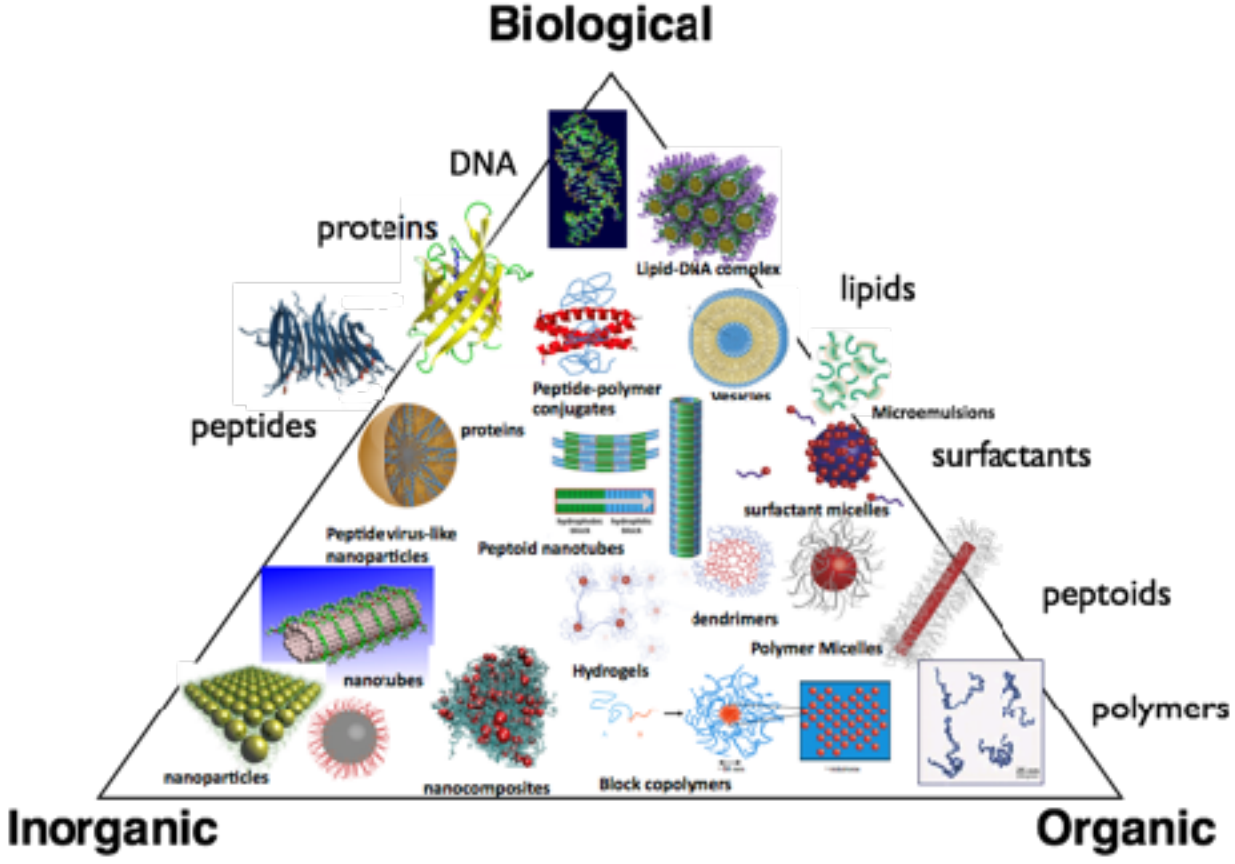
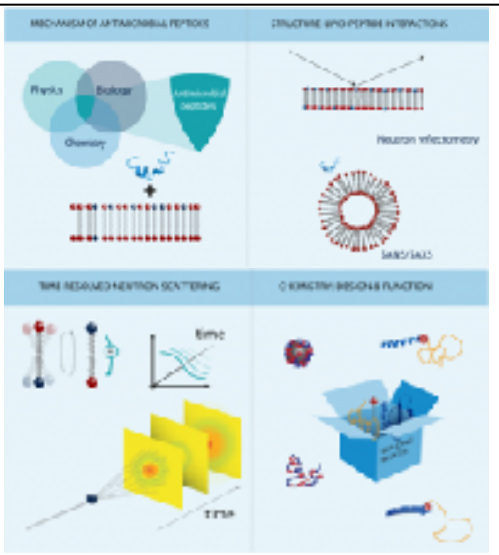


Photo: Arthur Sand.

Soft Matter group in Oslo: some ongoing projects

Mechanism of antimicrobial peptides



Beyond structural models for the mode of action: How natural antimicrobial peptides affect lipid transport J.E. Nielsen, V.A. Bjørnestad, V. Pipich, H. Jenssen, R. Lund. *Journal of colloid and interface science* 2021 582, 793-802

Impact of Antimicrobial Peptides on E. coli-mimicking Lipid Model Membranes: correlating structural and dynamic effects using scattering methods J.E. Nielsen, S. Prévost, H. Jenssen, R. Lund. *Faraday Discussions* 2020

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A biophysical study of the interactions between the antimicrobial peptide indolicidin and lipid model systems J.E. Nielsen, T.K. Lind, A. Lone, Y. Gerelli, P.R. Hansen, H. Jenssen, M. Cárdenas, R. Lund. *BBA-Biomembranes* 2019, 1861 (7), 1355-1364

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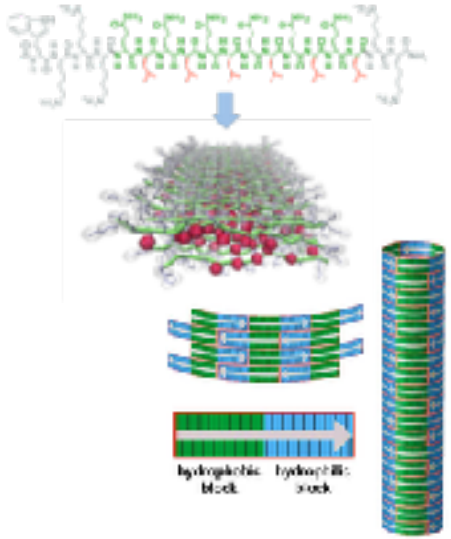
Novel peptide/peptoid-based nanostructures



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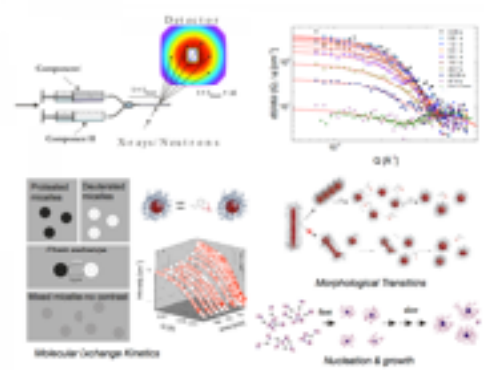
Structures and Kinetics Pathways of Self-assembly



How Detergents Dissolve Polymeric Micelles: Kinetic Pathways of Hybrid Micelle Formation in SDS and Block Copolymer Mixtures. S. Myhre, M. Amann, L. Willner, K. D Knudsen, R. Lund. *Langmuir* 2020, 36, 12887–12899.

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Cooperativity during Melting and Molecular Exchange in Micelles with Crystalline Cores N. König, L. Willner, V. Pipich, T. Zinn, R. Lund. *Physical Review Letters*. 122(7) .

Tale of Two Tails: Molecular Exchange Kinetics of Telechelic Polymer Micelles N. König, L. Willner, N. Mahmoudi, T. Zinn, R. Lund. *Physical Review Letters*. 124(19)

Kinetic Pathways for Polyelectrolyte Coacervate Micelle Formation Revealed by Time-Resolved Synchrotron SAXS M. Amann, J. Stensgaard Diget, J. Lyngsø, J.S. Pedersen, T. Narayanan, R. Lund. *Macromolecules*, 52 (21), 8227-8237

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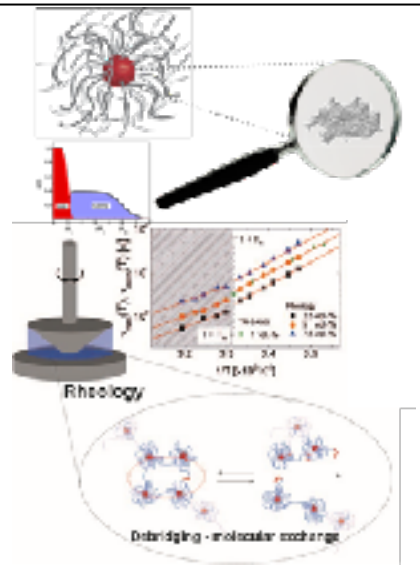
Polymers: micelles and hydrogels



Structure and thermodynamics of mixed polymeric micelles with crystalline cores: tuning properties via co-assembly N. König, L. Willner, R. Lund. Soft Matter. 15(39), 7777- 7786.

Spherical Micelles with Nonspherical Cores: Effect of Chain Packing on the Micellar Shape. N.König, L. Willner, G. Carlström, T. Zinn, K.D. Knudsen, F. Rise, D. Topgaard, R. Lund. Macromolecules. 53(23), s 10686- 10698

Cooperativity During Melting and Molecular Exchange in Micelles with Crystalline Cores. König, N.; Willner, L.; Pipich, V.; Zinn, T.; Lund, R. Phys. Rev. Lett. 2019, 122, 078001.

Telechelic Polymer Hydrogels: Relation between the Microscopic Dynamics and Macroscopic Viscoelastic Response. T. Zinn, L. Willner, R. Lund. *ACS Macro Lett.* 2016, 5, 12, 1353–1356.

Nanoscopic Confinement through Self-Assembly: Crystallization within Micellar Cores Exhibits Simple Gibbs-Thomson Behavior. T. Zinn, L. Willner, R. Lund. *Phys. Rev. Lett.* 113, 238305 (2014).

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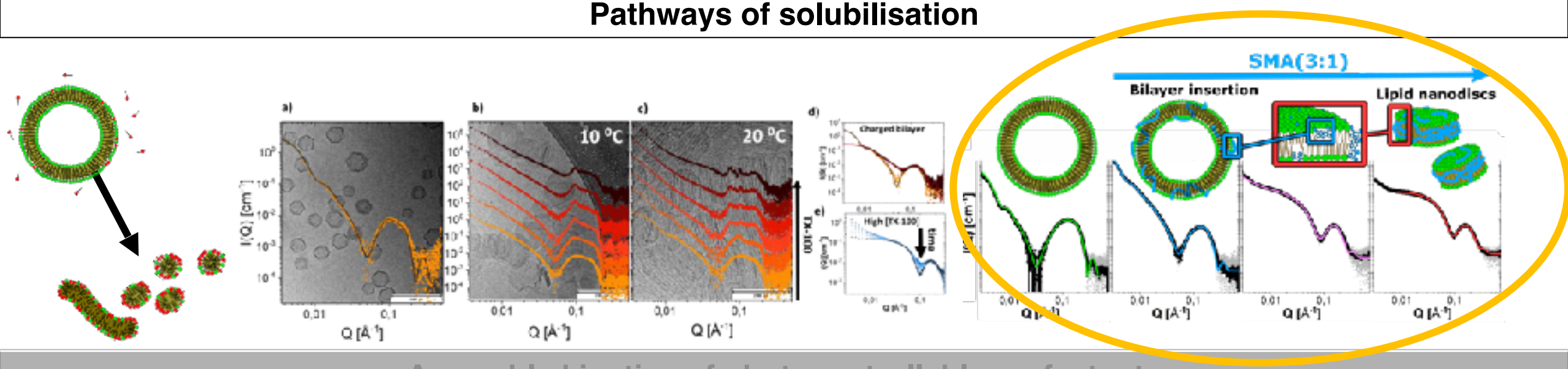
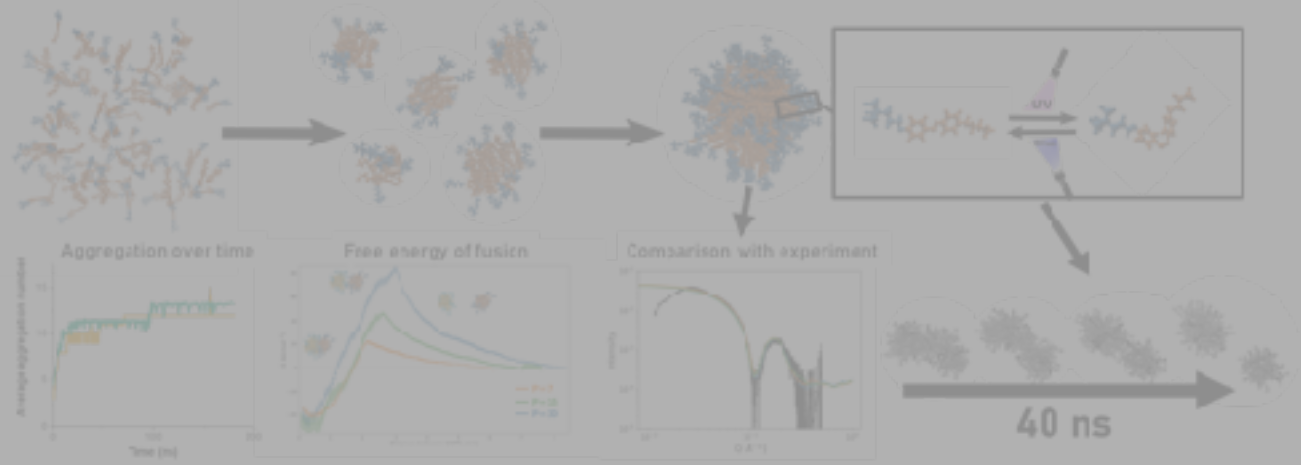
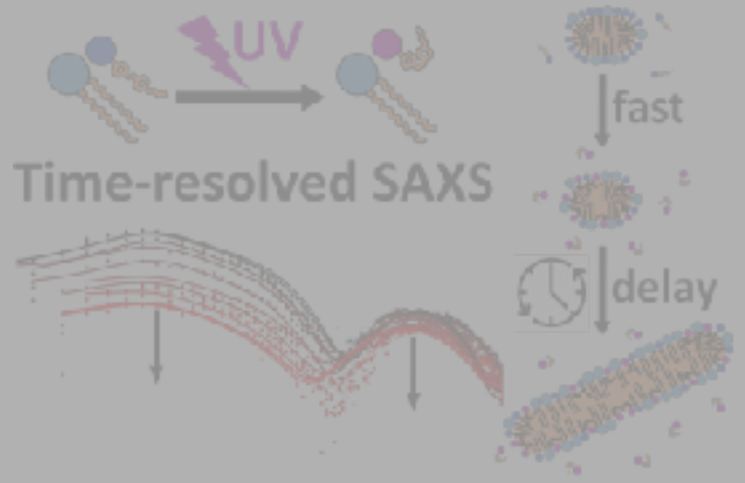
Soft Matter group in Oslo: Victoria´s PhD

Pathways of solubilisation



Assembly kinetics of photocontrollable surfactants

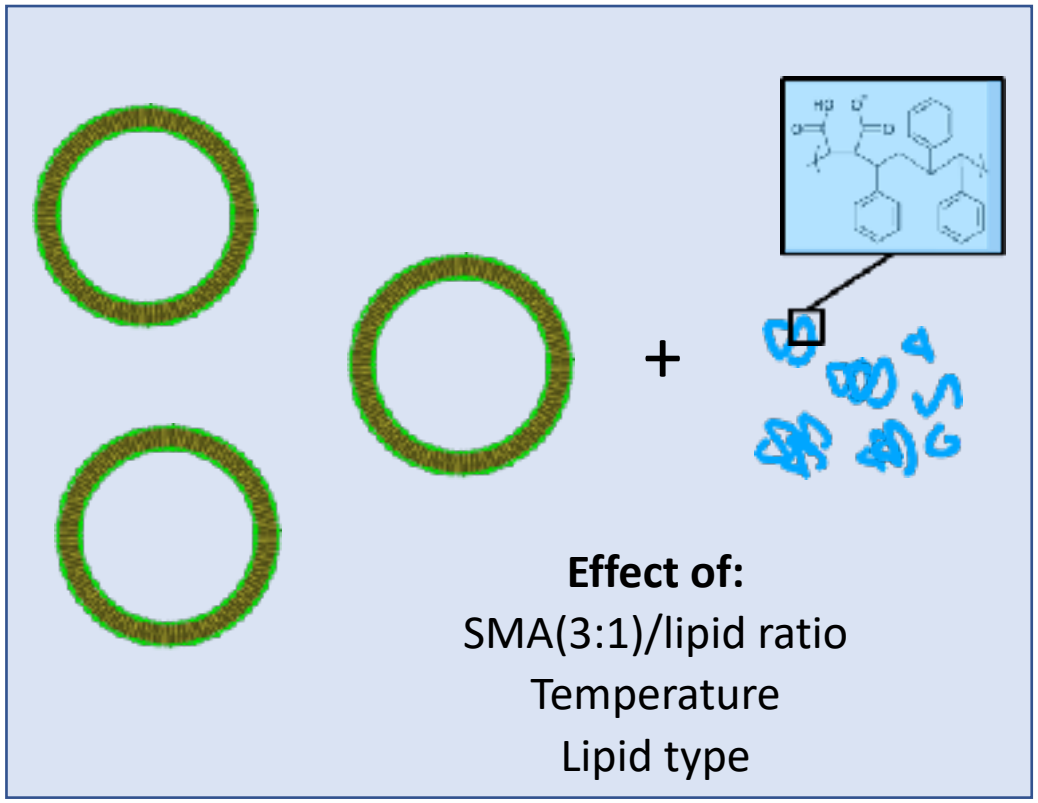




Motivation: understand the formation of nanodiscs

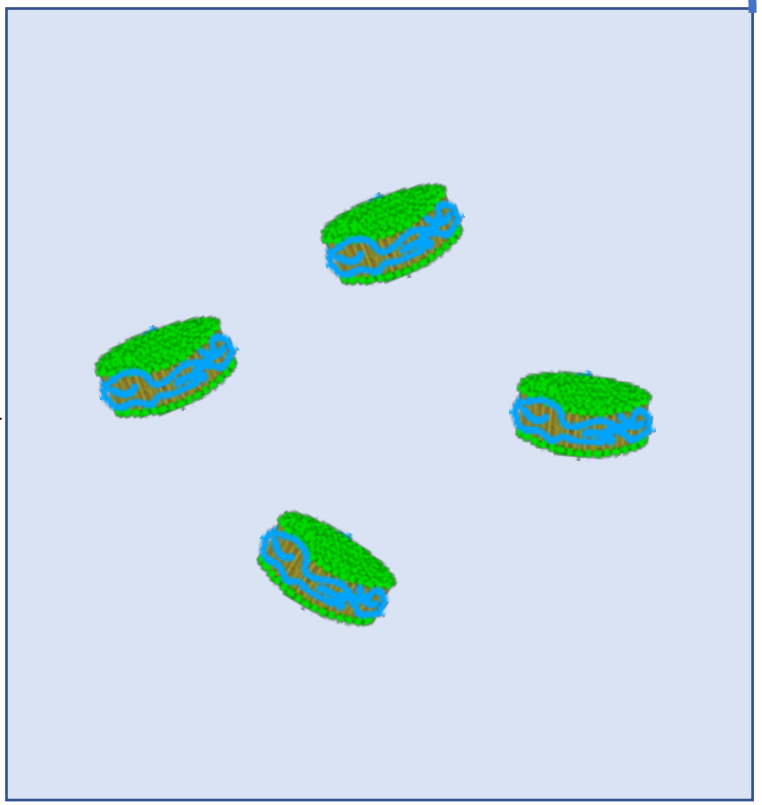
Structural characterization using **small angle X-ray scattering**

SMA(3:1) and lipid vesicle mixtures studied in solution

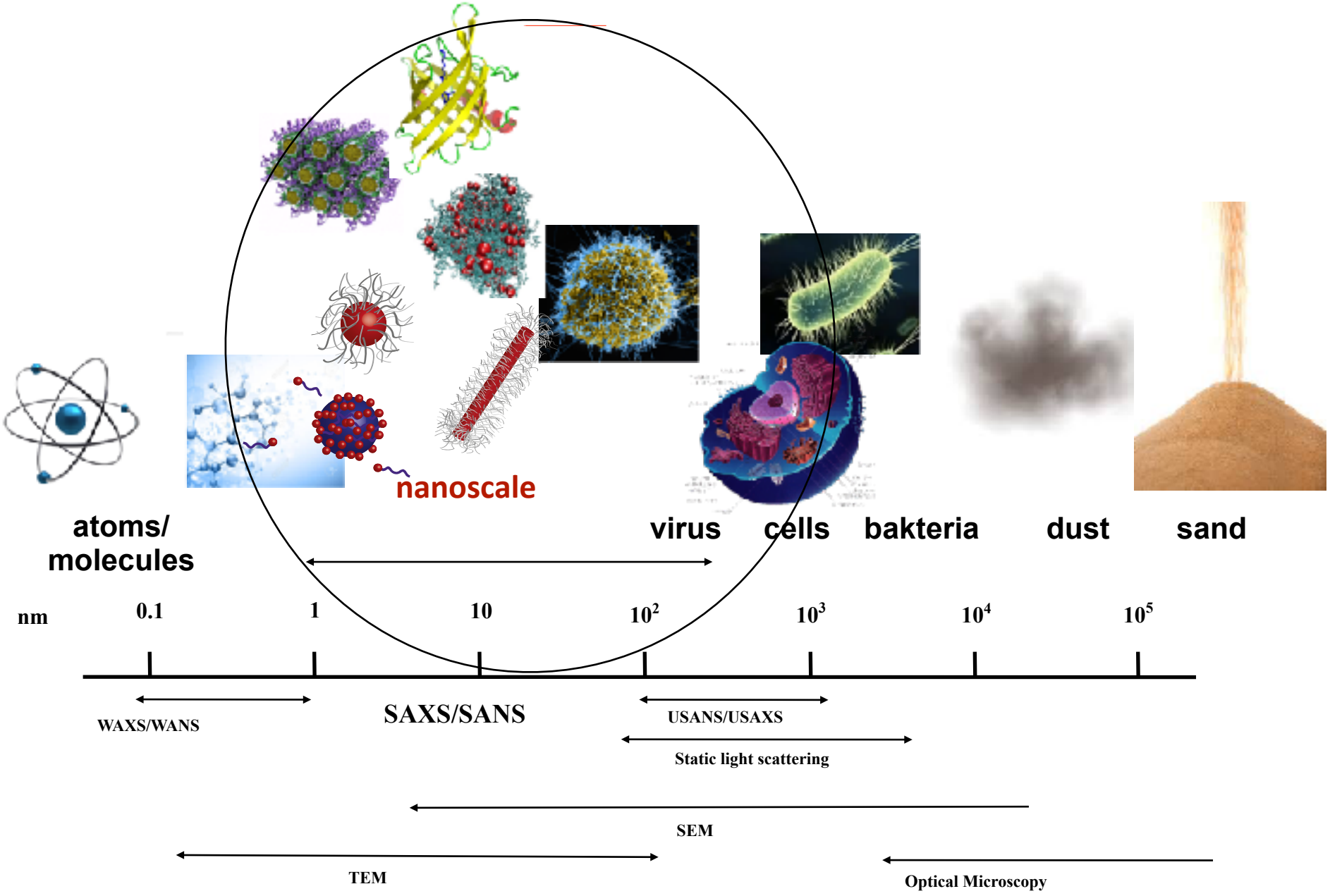


Intermediate structures in pathway

?



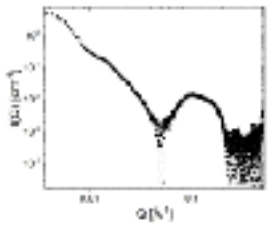
Soft and biological matter: length scales: ~1/Q



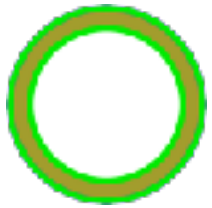
SAXS analysis

Analytical modelling

Normalized experimental data



Model in real space

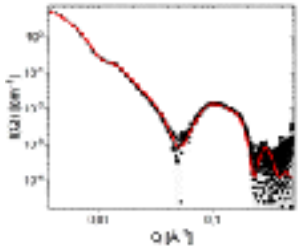


Model in Q-space

$$I(Q) = n_z \cdot V_p^2 \cdot \Delta\rho^2 \cdot P(Q) \cdot S(Q)$$

Includes known parameters (volume, electron density etc.) and unknow parameter (thicknesses, radius etc)

Comparison with experiment



Fit unknown parameters

Model fits

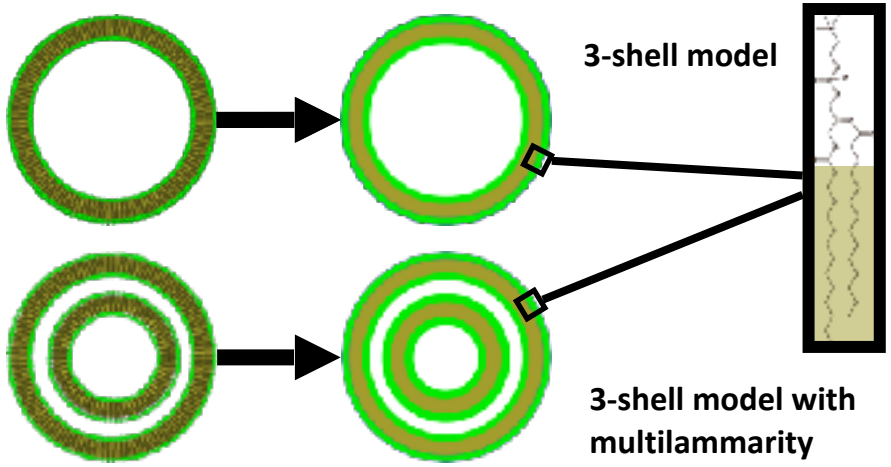
Finished!

Model does not fit

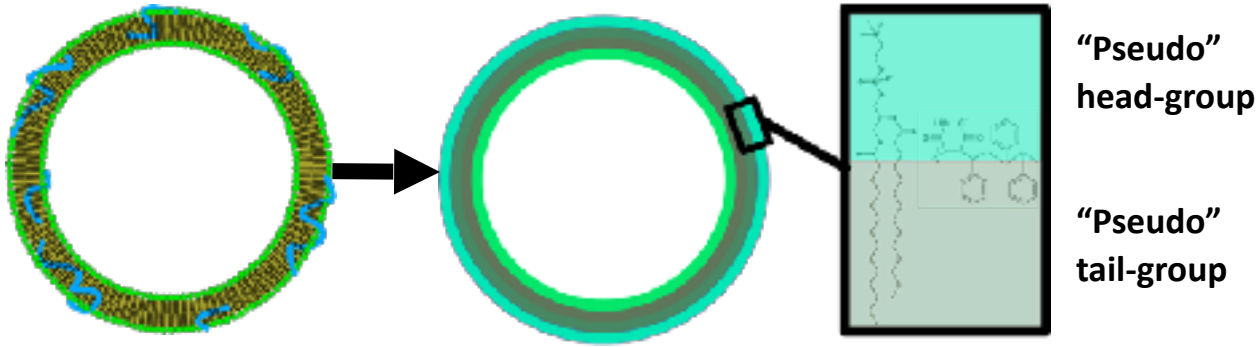
Investigate further with other methods

SAXS modelling: various shapes

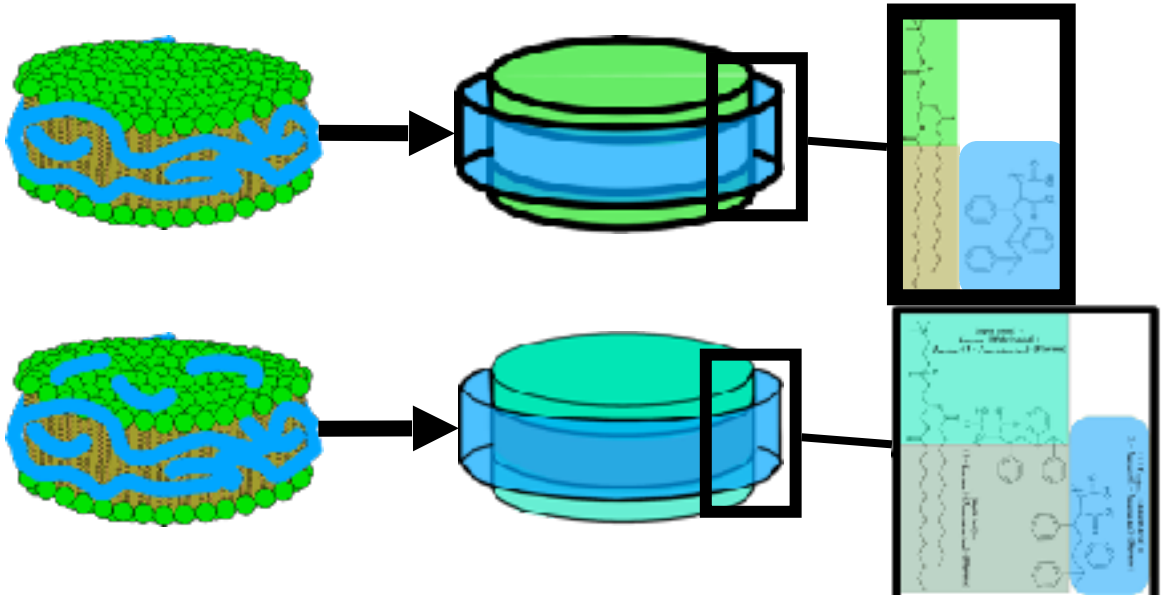
Vesicles



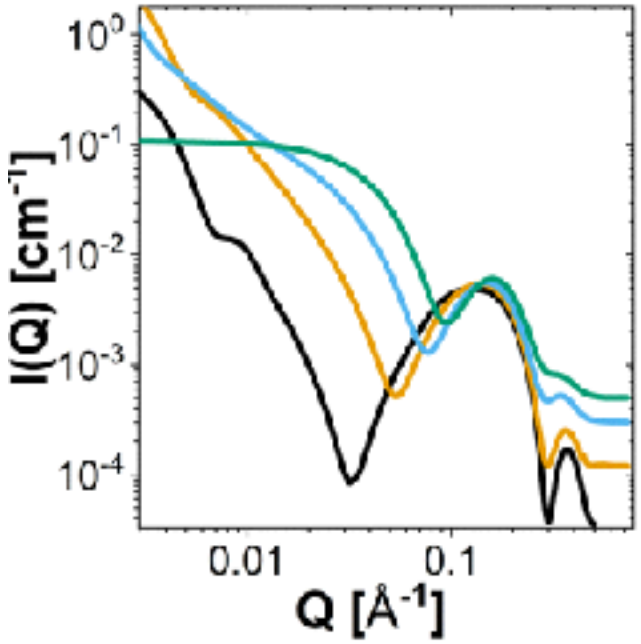
Vesicles with inserted polymers



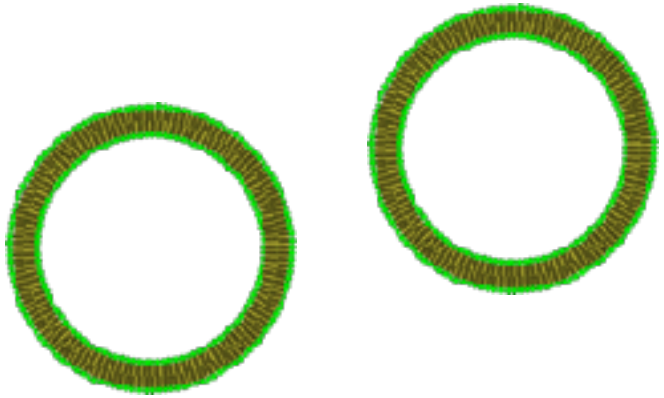
Nanodiscs



+ coexistence



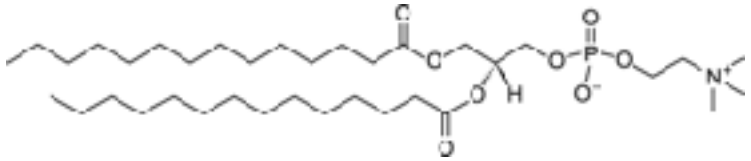
Experimental system



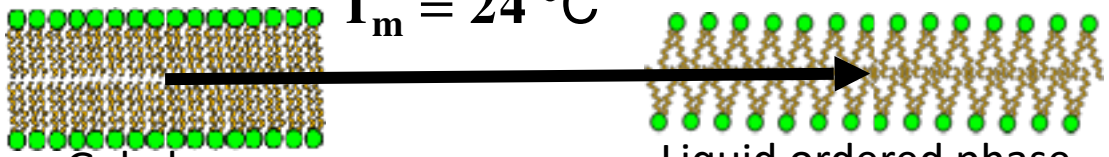
+

DESY

DMPC



$T_m = 24$ °C

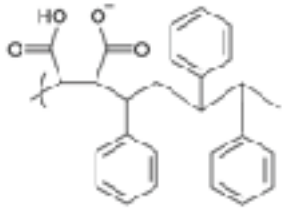


Gel phase

Liquid ordered phase

+

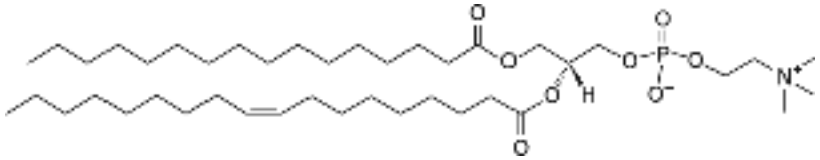
SMA 3:1



PDI=3.11

→ SAXS at 18 °C and 37 °C

POPC

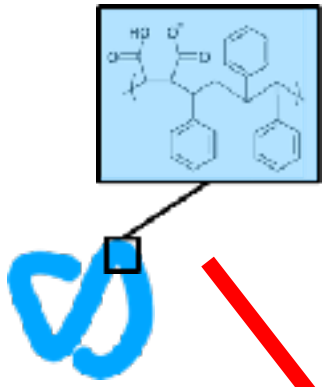


+

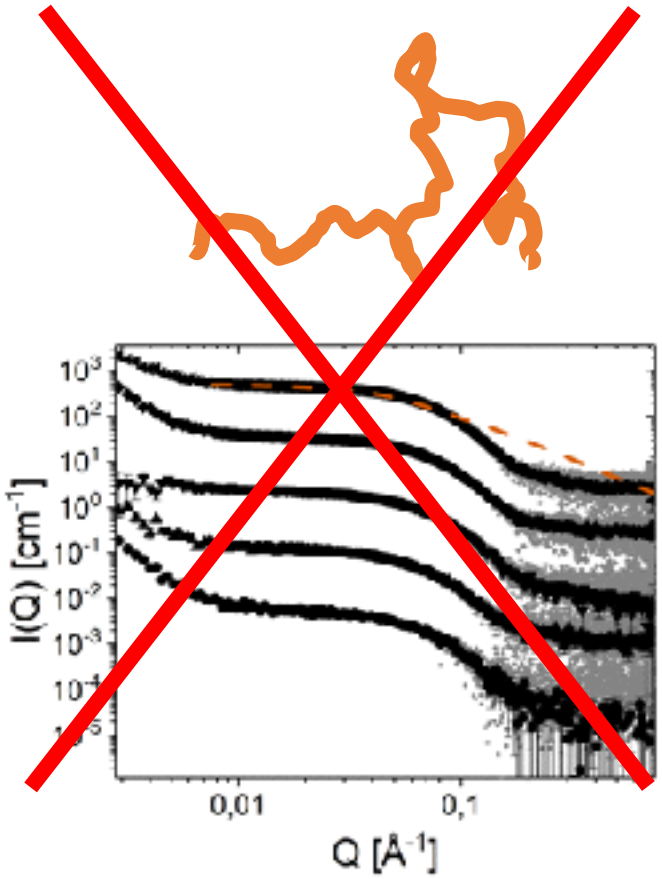
→ SAXS at 37 °C

SAXS: SMA polymer

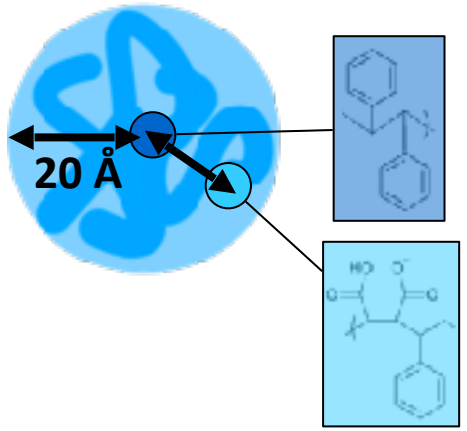
SMA(3:1) polymer in Tris buffer, 0.125M NaCl



Random coil

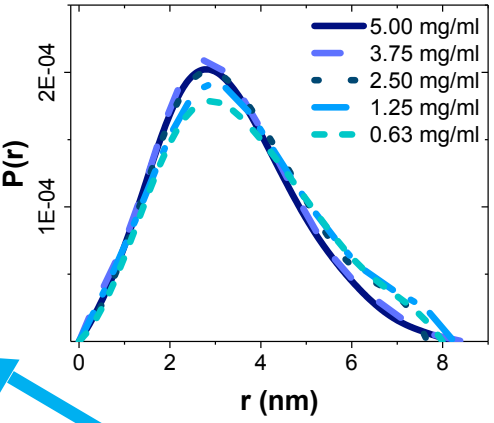


Globular collapsed structures («fuzzy spheres»)



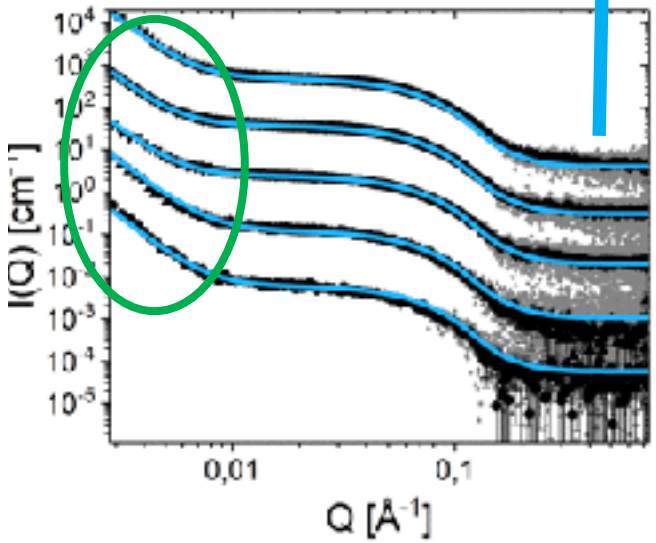
Concentration dependent background

Pair distribution function

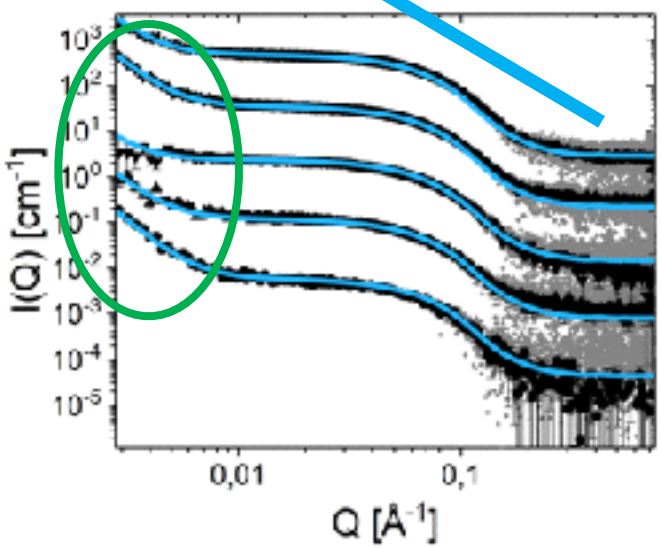


Larger aggregates

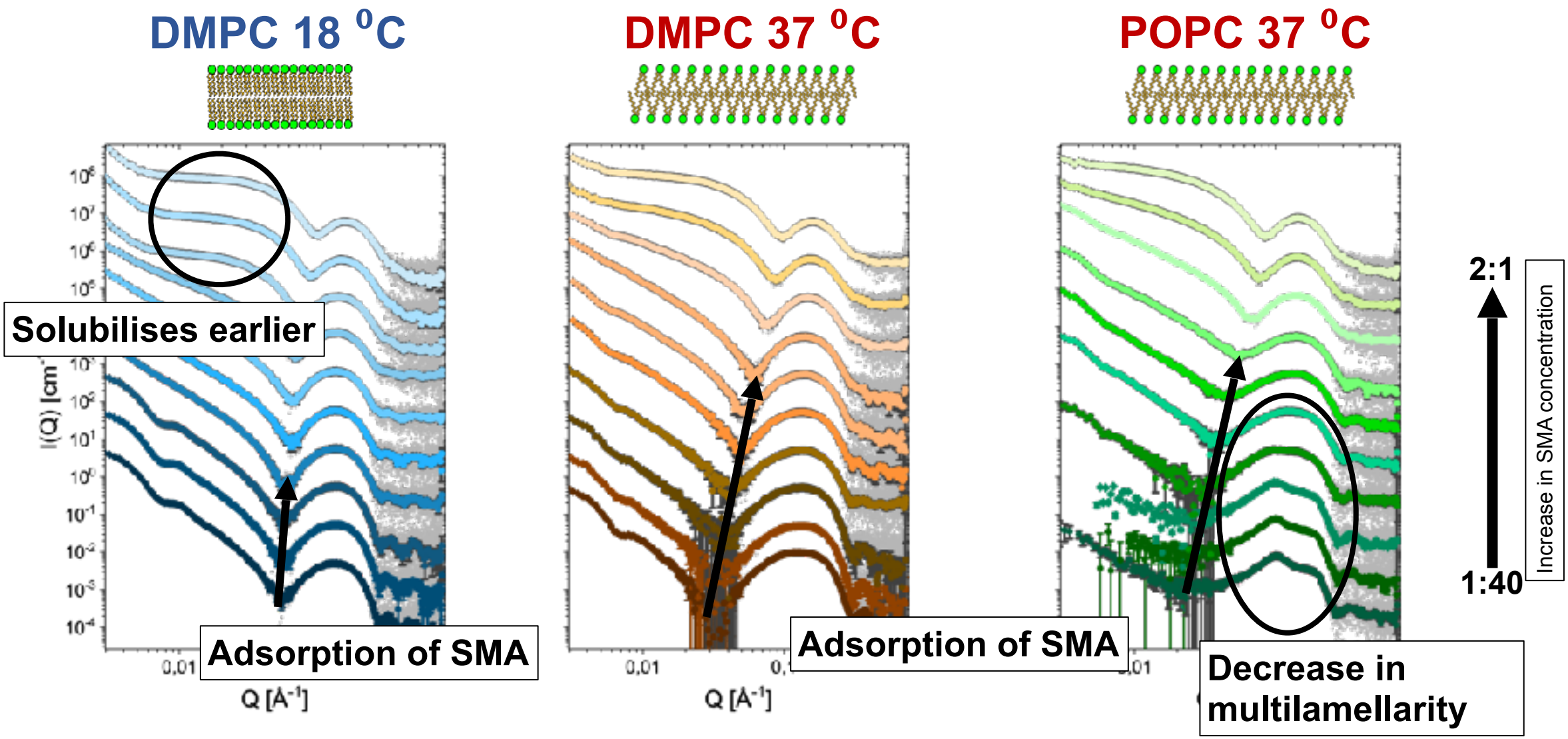
18 °C



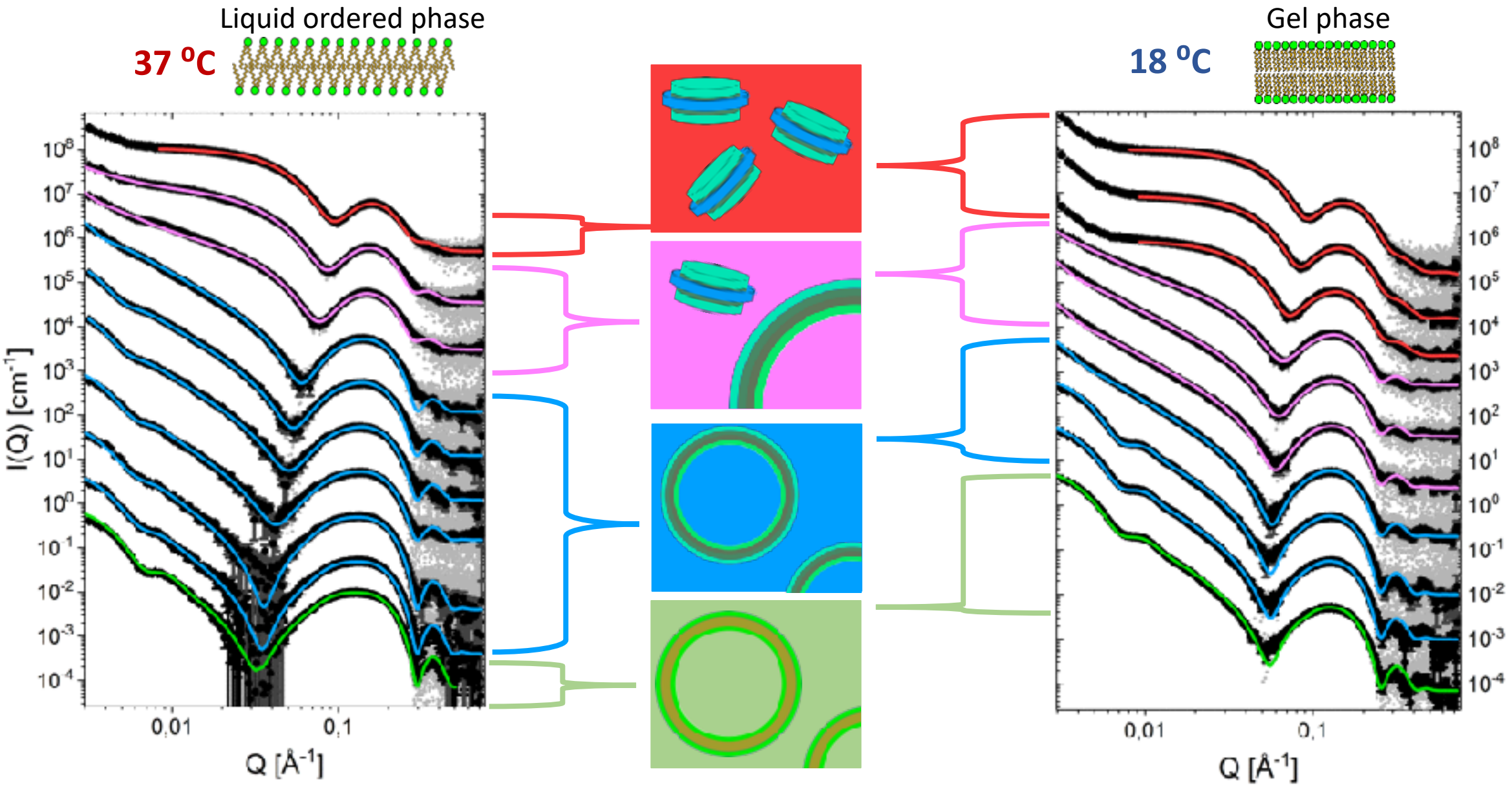
37 °C



SAXS : SMA/lipid vesicle mixtures

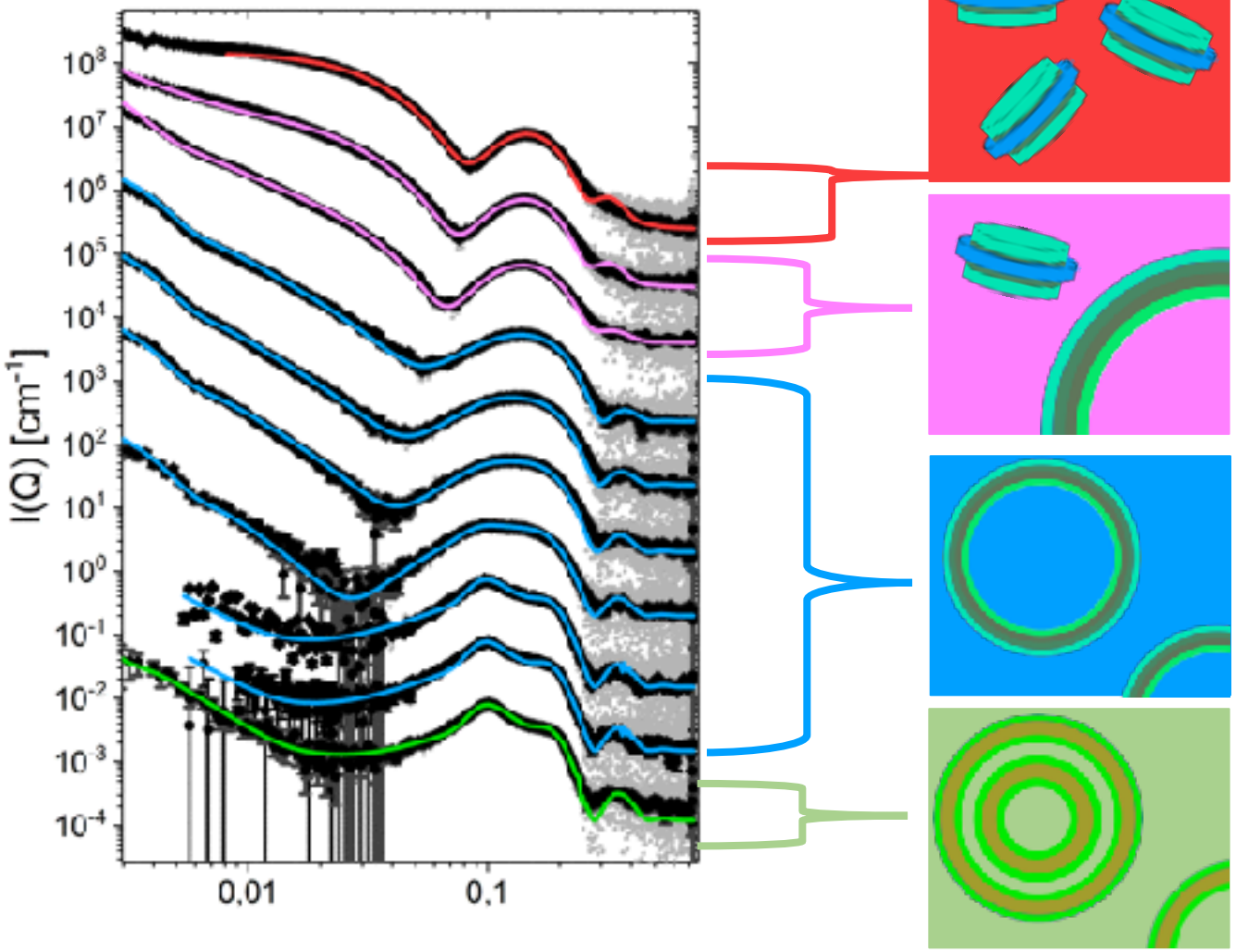


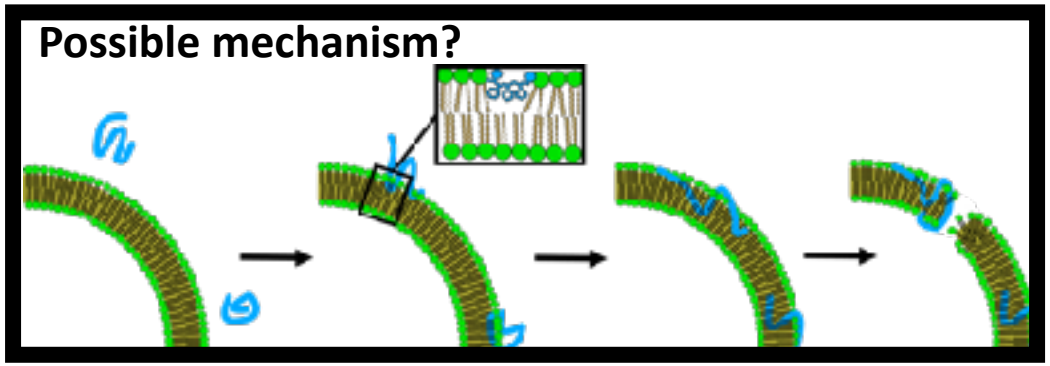
SAXS : SMA/lipid vesicle mixtures: DMPC

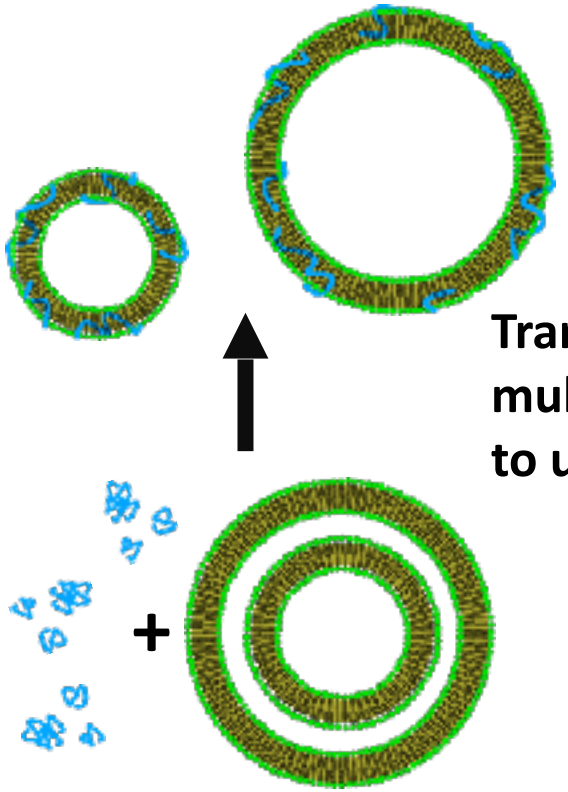


SAXS : SMA/lipid vesicle mixtures- POPC

37 °C





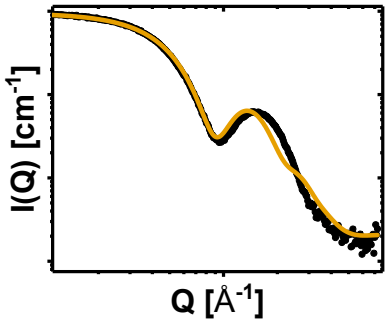


Transition from multilamellar structures to unilamellar structures

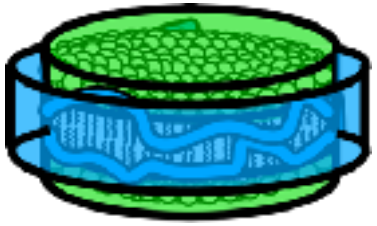
SAXS : SMA/lipid vesicle mixtures- other form factors

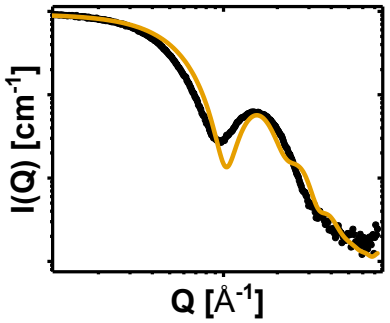
Other model candidates

Ellipsoidal core-shell mixed micelle

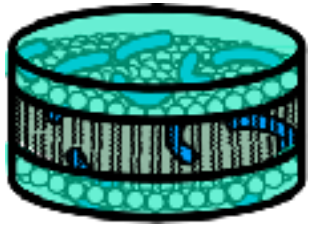


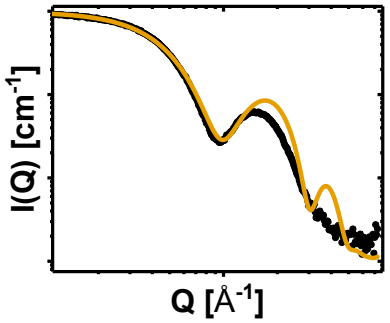
Lipid disc with SMA belt

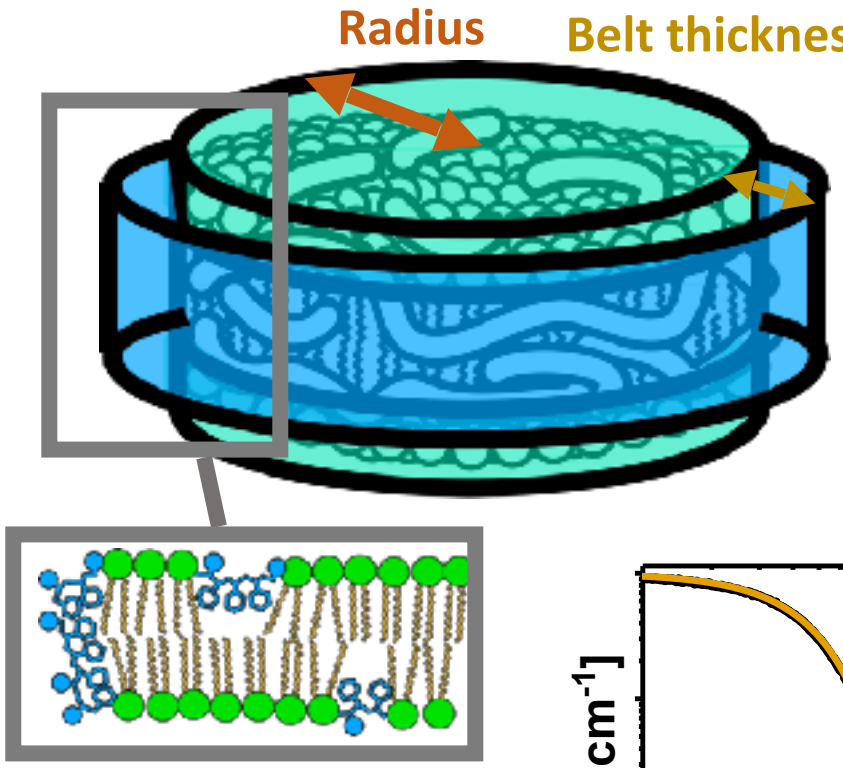


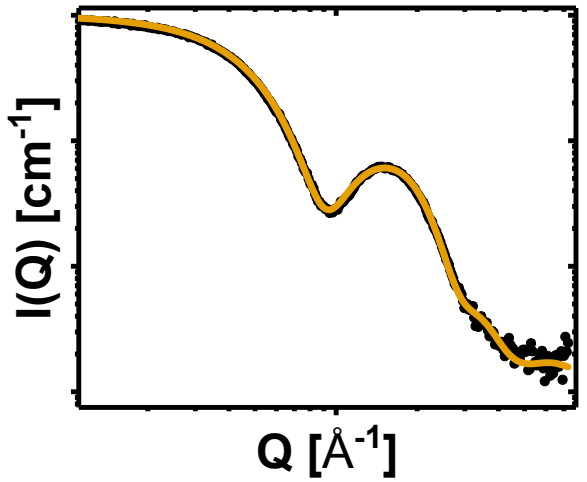


Mixed lipid:SMA disc



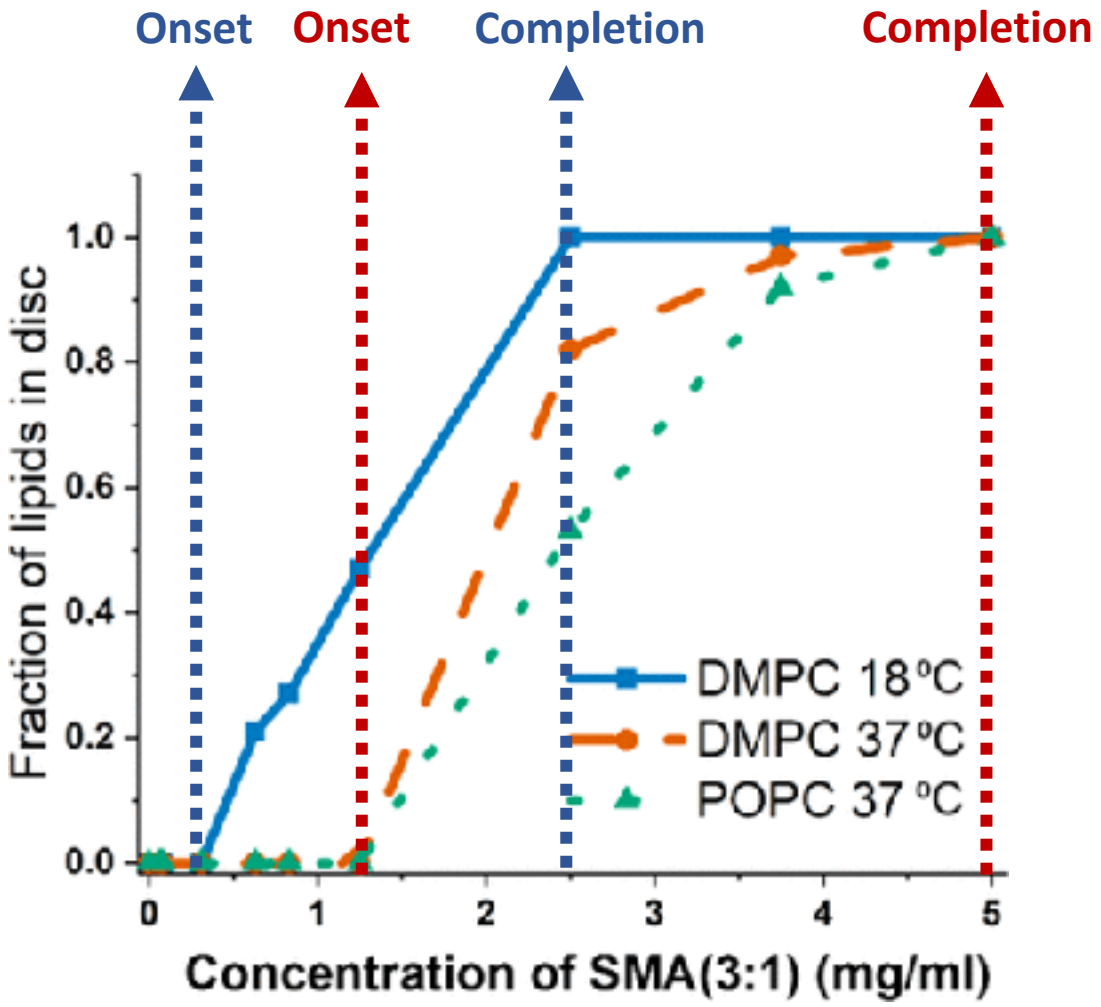






SMA/lipid vesicle mixtures: onset and completion of solubilisation

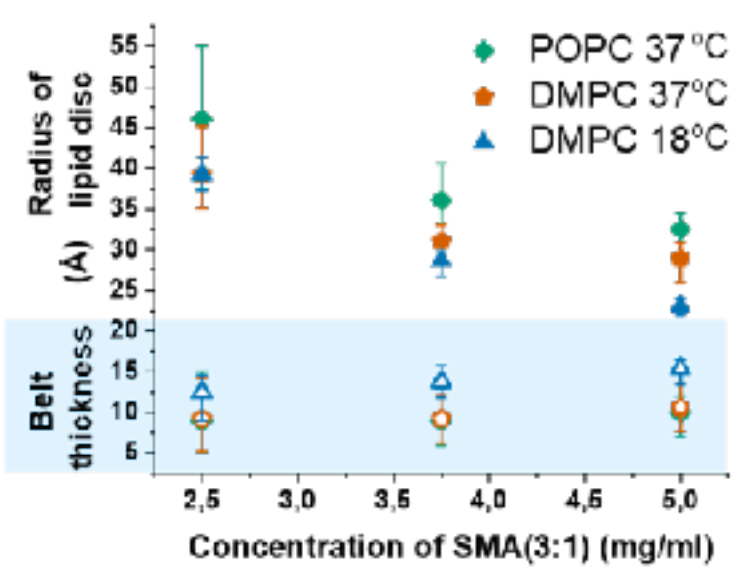
18 °C **37 °C**

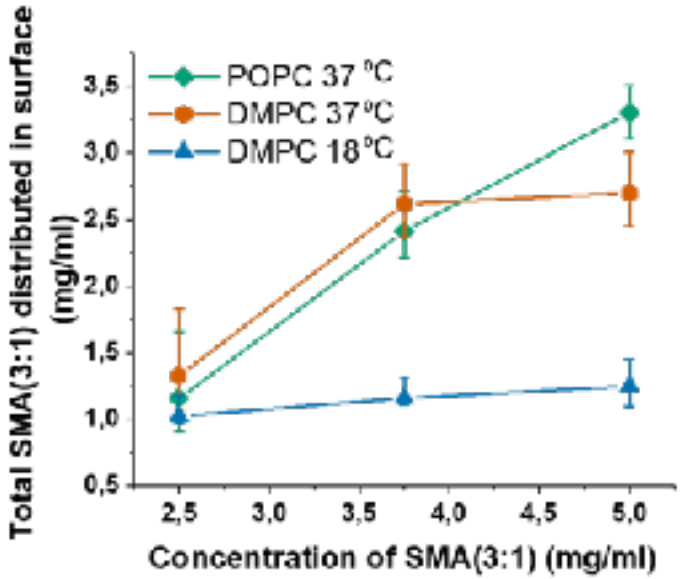


Onset and completion of solubilisation occurs at lower SMA(3:1) concentrations for DMPC below the transition temperature

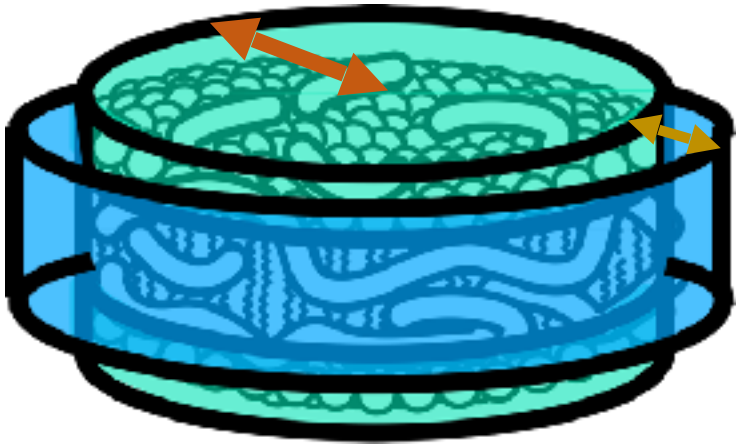
→ also found by Cuevas Arenas et al. using NMR and DLS (Nanoscale,2016,8,15016–15026)

SMA/lipid vesicle mixtures: structure of SMA:lipid nanodiscs

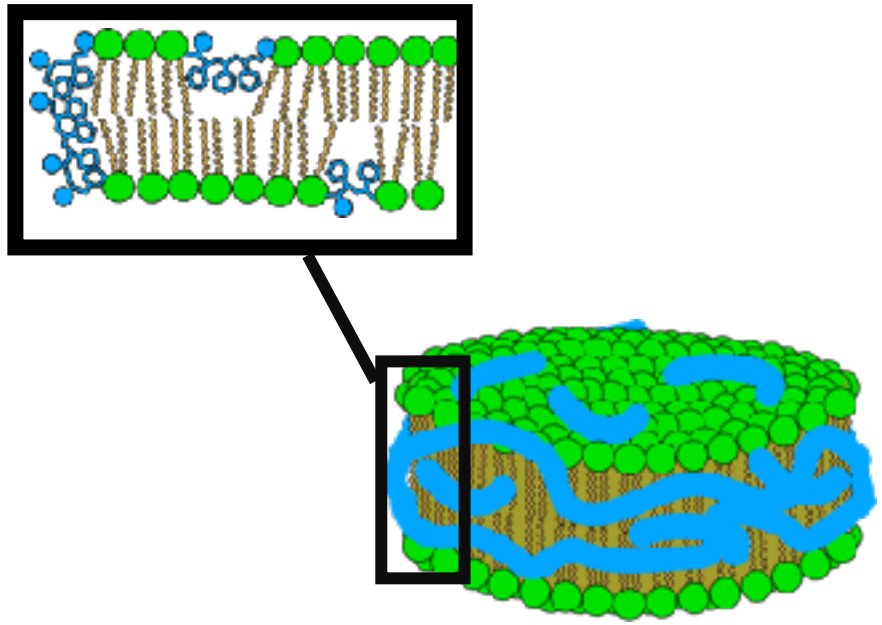


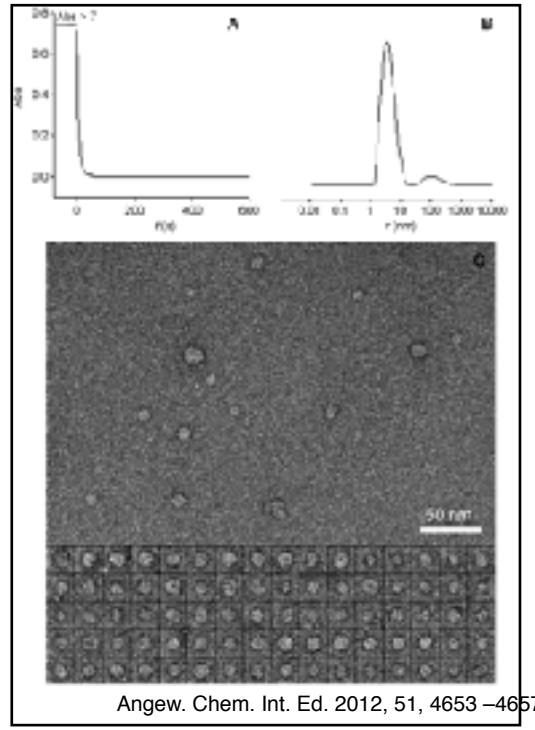


Radius (range) **Belt thickness (range)**



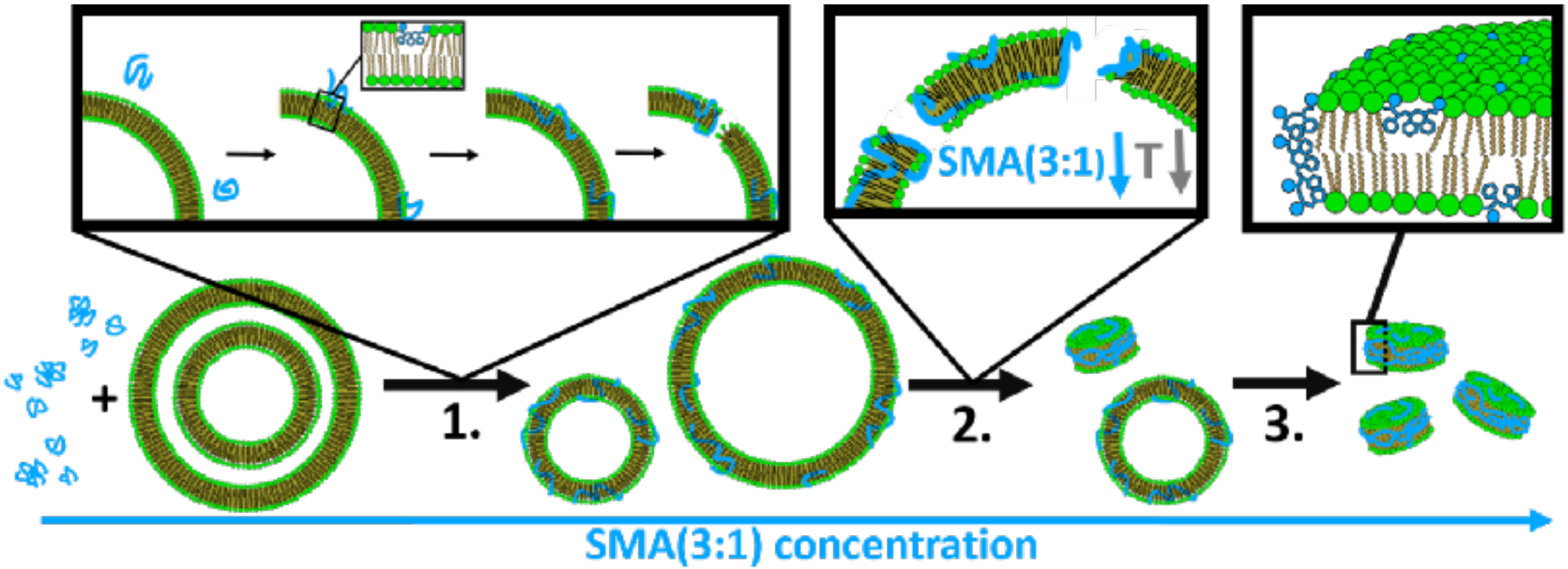
High polydispersity of sizes: PDI between 1.0 and 1.6
(σ(Gauss) between 0.31 and 0.24)





Angew. Chem. Int. Ed. 2012, 51, 4653 –4657

Conclusion



- Formation of nanodisc from lipid vesicles by SMA(3:1) largely follows the classical steps of solubilisation
- The bilayer fractures already before complete saturation occurs
- DMPC lipid bilayers are saturated and solubilised at lower SMA(3:1) concentrations when below the transition temperature
- POPC lipid have a higher resistance towards solubilisation by SMA(3:1) compared to DMPC
- Lipid acyl-chain packing is found to be disrupted by SMA(3:1) insertion
- Lateral distribution of SMA(3:1) in the surface of the bilayer persists in the solubilised discs – only excess SMA(3:1) forms the belt.

Ackowledgement

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Understanding the Structural Pathways for Lipid Nanodisc Formation: How Styrene Maleic Acid Copolymers Induce Membrane Fracture and Disc Formation

Victoria Ariel Bjørnestad, Marcella Orwick-Rydmark, and Reidar Lund*

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Thanks, takk..!

also present in the formed discs, with excess copolymer distributed along the normal of the bilayer. The size and SMA distribution in the resulting discs strongly depend on the temperature, lipid/copolymer ratio, and lipid type. We find that the solubilization limit increases for membranes above the melting point, suggesting that defects in gel-like lipid membranes play a significant role in membrane fracturing and nanodisc formation. These findings provide unique insights into the formation of nanodiscs as well as into the microscopic mechanism of solubilization, which plays an important role in many applications and products ranging from household goods to biotechnology and medicine.