Bilayers at the ILL

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Dynamic polymer-based nanodiscs for membrane biophysics

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Amphiphilic copolymers enable a fundamentally new approach for investigating membrane proteins, as they obviate the use of conventional detergents. These polymers extract proteins and surrounding lipids directly from cellular membranes to form nanosized discs, where the polymer wraps around a lipid-bilayer patch. Such nanodiscs are amenable to a broad range of methods requiring nanosized particles, which sets them apart from traditional bilayer systems such as vesicles. In this talk, I will focus on styrene/maleic acid (SMA) and diisobutylene/maleic acid (DIBMA) co-polymers as well as derivatives thereof that display improved properties over existing polymers.

Particular attention will be paid to the dynamic nature of polymer-encapsulated nanodiscs, which exchange their lipid contents rapidly through collisional transfer. This was shown by both temperature-dependent stopped-flow small-angle neutron scattering (SANS) experiments at ILL and concentration-dependent stopped-flow Förster resonance energy transfer (FRET) assays (Cuevas Arenas et al. *Sci. Rep.* **2017**, *7*, 45875; Grethen et al. *J. Membr. Biol.* **2018**, *251*, 443; Danielczak et al. *Eur. Polym. J.* **2018**, *10*, 206). Moreover, we used differential scanning calorimetry (DSC), Raman scattering, and time-resolved fluorescence spectroscopy to demonstrate that DIBMA does not disturb the order, dynamics, and hydration of the solubilised mem-brane fragments (Oluwole et al. *Angew. Chem. Int. Ed.* **2017**, *56*, 1919; Grethen et al. *Sci. Rep.* **2017**, *7*, 11517; Oluwole et al. *Langmuir* **2017**, *33*, 14378). Finally, new, modified polymers offer additional advantages in that they carry no charge and have been optimised for membrane-protein extraction from popular expression hosts.

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