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How charges effect the solubilisation of artificial and native membranes by amphiphilic copolymers

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Certain amphiphilic copolymers form lipid-bilayer nanodiscs from artificial and natural membranes, thereby rendering incorporated membrane proteins optimal for structural analysis. Recent studies have shown that the amphiphilicity of a copolymer strongly determines its solubilization efficiency. This is especially true for highly negatively charged membranes, which experience pronounced Coulombic repulsion with polyanionic polymers. Here, we present a systematic study on the solubilization of artificial multicomponent lipid vesicles that mimic inner mitochondrial and fungal membranes, which harbor essential membrane-protein complexes. In particular, we compared the lipid-solubilization efficiencies of established anionic with less densely charged or zwitterionic and even cationic copolymers in low- and high-salt concentrations. The nanodiscs formed under these conditions were characterized by dynamic light scattering and negative-stain electron microscopy. Overall, our results show that some recent, zwitterionic copolymers are best suited to solubilize negatively charged membranes at high ionic strengths even at low polymer/lipid ratios [1].

As a proof of principle, we describe an efficient recovery of protein-encapsulating nanodiscs from membranes of *Chaetomium thermophilum*, a thermophilic fungus. We identified ~600 proteins by mass spectrometry and obtained two 3D reconstructions from cryo-EM for the nanodisc-containing cell extract. With this combined methodological approach, we provide a deeper understanding of eukaryotic membrane proteomes [2].

[1] K. Janson *et al.* Biochim. et Biophys. Acta, Biomembr. 1863, **2021**, 183725.

[2] K. Janson *et al.* Biomacromolecules 23, **2022**, 5084-5094.