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Rational Approaches in Structure Determination of Membrane Proteins. P Nissen, J.P. Morth, B.P. Pedersen, T.L. Sorensen, Dept. Molecular Biology, Univ. Aarhus, Aarhus C, Denmark.

Implementation of high-throughput methods in protein crystallography ranging from cloning, expression and purification of targets, to crystallization, data collection, phasing and model building is gradually spreading into the crystallographic community. However difficult, yet highly important targets in the life sciences, such as membrane proteins and large complexes, do not readily fit into this pipeline, and present large challenges at all stages of the structure determination process, crystallization not the least ^[1]. Determination of such structures thus calls for highly dedicated efforts and unique solutions. The use of selenomethionine MAD/SAD phasing will not be possible for membrane proteins isolated from native tissue or advanced expression systems, and “classical” heavy-metal derivatives must be applied in such cases. This is particularly challenging when applied to small, fragile crystals with weak diffraction properties. However, the aforementioned development of the available technologies combined with data mining of the growing data base offer specific opportunities to design rational and efficient experimental strategies in crystallization and phasing of membrane proteins ^[2].

[1] Sorensen TL, Olesen C, Jensen AM, Moller JV, Nissen P (2006). Crystals of sarcoplasmic reticulum Ca(2+)-ATPase. *J Biotechnol.* epub ahead of print.

[2] Morth JP, Sorensen TL, Nissen P. Membrane's eleven: heavy-atom derivatives of membrane protein crystals. *Submitted*