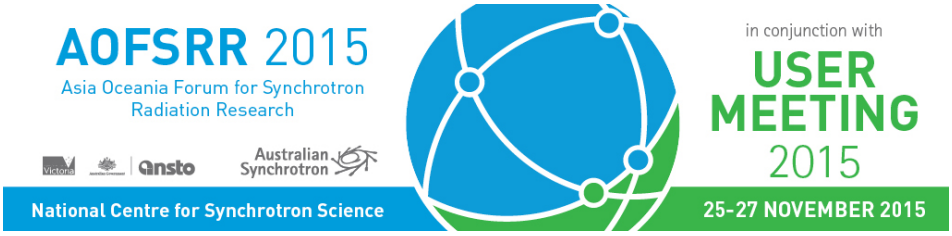

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Exploring the *in meso* crystallization mechanism by using synchrotron Small Angle X-ray Scattering

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Recently, the development of a novel *in meso* crystallization method has facilitated the structural determination of several biologically relevant membrane proteins (MPs). However, *in meso* crystallization remains poorly understood as MPs are difficult to express and handle. An improved understanding of this technique can lead to an improved success rate and facilitate the structural determination of more MPs. These structures are important for rational drug design and designing new treatments for a wide range of diseases.
Bicontinuous cubic phases are the most commonly used lipid phases for *in meso* crystallization. The proposed mechanism states that the membrane protein or peptide is initially uniformly dispersed in the cubic phase but that crystals grow from a local lamellar phase which acts as a conduit between the crystal and the bulk cubic phase. However, there is very limited experimental evidence for this theory. In this work we have explored this by characterizing the lipid mesophase microenvironment by using synchrotron Small Angle X-ray Scattering with a micro-sized beam during crystal growth of the DAP12-TM peptide of which the structure was recently solved. Crystal growth was indeed found to occur from the cubic mesophase, and a highly-oriented local lamellar phase was observed consistent with the co-location of the lamellar phase at a crystal face supporting the proposed mechanism for in meso crystallization. A new observation of this study is that some crystals may give rise to diffraction at wide angles which is of potential use in locating these crystals.

Keywords

SAXS, *in meso* crystallization, bicontinuous cubic phase

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