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ORAL ABSTRACT PRESENTATIONS

SESSION TITLE: APPLICATIONS OF CRYO-EM IN MEDICINE

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Abstract OR-14: Fibril Structure and Interface Polymorphism of Amyloid- β (1-42)

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Background: Amyloids are associated with many diseases. The recent breakthrough in the cryo-EM technique has made it possible to study the structure of amyloid fibrils by cryo-EM to high resolution. The technique will be introduced and applications to different amyloid structures presented, in particular the structure of the amyloid- β fibril (A β 1-42), which is involved in Alzheimer's disease. Furthermore, new image processing methods will be presented to reconstruct macromolecular motions from single-particle image data.

Methods: Single-particle cryo-EM was used to determine helical reconstructions of different fibrillar structures. Furthermore, an approach is presented to determine the principal motions of macromolecules from single-particle data.

Typical classification methods aim for maximizing density differences between different models. However, density variance is not the same as conformational variance (i.e. variance of atomic model coordinates), and for interpreting molecular motions, conformational variance is most relevant. We present an approach to determine this conformational variance.

Results: The structure of an amyloid- β fibril (A β 1-42) and polymorphs of it were determined. In addition, the structure of an SH3 amyloid fibril is presented, which has been extensively studied as a model system for amyloid formation.

Conclusion: Cryo-EM reveals high-resolution structural details of amyloid fibrils.

Key Words: amyloid fibrils • helical reconstruction • Alzheimer disease

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