

MS16-1-5 Amyloid beta 42 fibrils: a small-angle X-ray scattering view of the growth kinetics and its variability
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Abstract

Aggregation of the peptide amyloid beta 42 (A β 42) into fibrils is a key event in the pathogenesis of Alzheimer's disease. During this aggregation process, smaller neurotoxic A β 42 oligomers are formed, which, despite their relevant role in neurodegeneration, are insufficiently characterized [1]. We employed synchrotron time-resolved Small-angle X-ray Scattering (TR-SAXS) to monitor the kinetics of A β 42 aggregation in solution including structural information. Multiple TR-SAXS datasets spanning several hours of the aggregation process were collected and could be adequately described in terms of a minimal set of coarse-grained structures, revealing the overall features of the oligomers. Moreover, the inherent variability of the process was addressed, and the A β 42 fibrils present at late stages were compared with those present in the literature [2,3,4].

References

- [1] Haass, Christian, and Dennis J. Selkoe. "Soluble protein oligomers in neurodegeneration: lessons from the Alzheimer's amyloid β -peptide." *Nature reviews Molecular cell biology* 8.2 (2007): 101-112.
- [2] Langkilde, Annette E., et al. "The architecture of amyloid-like peptide fibrils revealed by X-ray scattering, diffraction and electron microscopy." *Acta Crystallographica Section D: Biological Crystallography* 71.4 (2015): 882-895.
- [3] Wälti, Marielle Aulikki, et al. "Atomic-resolution structure of a disease-relevant A β (1–42) amyloid fibril." *Proceedings of the National Academy of Sciences* 113.34 (2016): E4976-E4984.
- [4] Lattanzi, Veronica, et al. "Amyloid β 42 fibril structure based on small-angle scattering." *Proceedings of the National Academy of Sciences* 118.48 (2021).

Amyloid growth kinetics monitored by SAXS

