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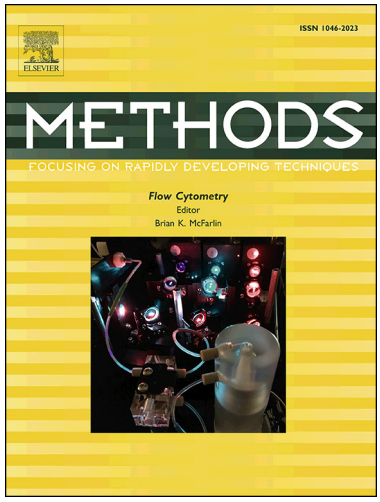

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3D Structure Determination of Amyloid Fibrils using Solid-State NMR Spectroscopy

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ABSTRACT:
The amyloid fold is structurally characterized by a typical cross-β architecture, which is under debate to represent an energy-favourable folding state that many globular or natively unfolded proteins can adopt. Being initially solely associated with amyloid fibrils observed in the propagation of several neurodegenerative disorders, the discovery of non-pathological (or "functional") amyloids in many native biological processes has recently further intensified the general interest invested in those cross-β supramolecular assemblies. The insoluble and non-crystalline nature of amyloid fibrils and their usually inhomogeneous appearance on the mesoscopic level pose a challenge to biophysical techniques aiming at an atomic-level structural characterization. Solid-state NMR spectroscopy (SSNMR) has granted breakthroughs in structural investigations on amyloid fibrils ranging from the assessment of the impact of polymorphism in disease development to the 3D atomic structure determination of amyloid fibrils. First landmark studies towards the characterization of atomic structures and interactions involving functional amyloids have provided new impulses in the understanding of the role of the amyloid fold in native biological functions.
Over the last decade many strategies have been developed in protein isotope labelling, NMR resonance assignment, distance restraint determination and 3D structure calculation of amyloid fibrils based on SSNMR approaches. We will here discuss the emerging concepts and state-of-the-art methods related to the assessment of amyloid structures and interactions involving amyloid entities by SSNMR.

Keywords:
Solid-state NMR, Amyloid fibrils, Structural biology, Protein aggregation, Prions, Structure calculation, Isotopic labelling, Proton detection

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