



GESELLSCHAFT
DEUTSCHER CHEMIKER

KOLLOQUIUM

Terminänderung!!

Wintersemester 2025/26

Titel

Aggregation kinetics and amyloid fibril structure probed by solution and MAS solid-state NMR spectroscopy

Vortragender

Prof. Dr. Bernd Reif

Technische Universität München (TUM), Department Chemie, Lichtenbergstr. 4, 85747 Garching, Germany; Helmholtz-Zentrum München (HMGU), Ingolstädter Landstr. 1, 85764 Neuherberg, Germany

Abstract

Protein deposits consist primarily of the amyloid protein, but can contain other factors such as lipids, proteoglycans, and chaperones. So far, it is unclear how the cellular environment modulates fibril polymorphism and how differences in fibril structure affect cell viability. In the past, we investigated the structural properties of Alzheimer's disease A β and Diabetes type II hIAPP (human islet amyloid polypeptide) fibrils. Both fibril structures contain unstructured regions which are potential interaction sites for chaperones, but might as well be important for seeding involving secondary nucleation. The small heat-shock protein (sHSP) α B-Crystallin (α BC) is abundant in brains of AD patients, and colocalizes with A β amyloid plaques. We find that α BC prevents the generation of a compact fibril structure and leads to the formation of a new polymorph with a dynamic N-terminus. We compared biophysical experiments, such as ThT amyloid fibril aggregation kinetics and MAS solid-state NMR data to yield insights into the structural mechanisms of fibril polymorphism. Using MAS solid-state spectroscopy, we investigated the N-terminal region of hIAPP fibrils that is elusive in all cryo-EM structures that have been determined till to-date. A comparative analysis between wild-type hIAPP and a disulfide-deficient variant hIAPP(C2S,C7S) unveils a shared fibril core structure, yet strikingly distinct dynamics in the N-terminus. The variant fibrils lacking the disulfide bond exhibit an extended β -strand conformation which might facilitate surface nucleation. The role of the N-terminus in modulating secondary nucleation rates is discussed.

References

Rodina N, Hornung S, Sarkar R, Suladze S, Peters C, Schmid PWN, Niu Z, Haslbeck M, Buchner J, Kapurniotu A, Reif B (2024) Modulation of Alzheimer's Disease A β 40 Fibril Polymorphism by the Small Heat Shock Protein α B-Crystallin. J. Am. Chem. Soc. 146: 19077-19087.
Suladze S, Sustay Martinez C, Rodriguez Camargo DC, Engler J, Rodina N, Sarkar R, Zacharias M, Reif B (2024) Structural Insights into Seeding Mechanisms of hIAPP Fibril Formation. J. Am. Chem. Soc. 146: 13783-13796.
Suladze S, Sarkar R, Rodina N, Bokvist K, Krewinkel M, Scheps D, Nagel N, Bardiaux B, Reif B (2024) Atomic resolution structure of full-length human insulin fibrils. Proc. Natl. Acad. Sci. USA 121: e2401458121.

Ort

Chemie, HS1 – Campus Nord, Otto-Hahn-Straße 6

Anfahrt: <http://www.ewit.ccb.tu-dortmund.de/gdch/anfahrt.html>

Zeit

Dienstag, 27.01.2026, Seminar 14.00 Uhr, Vortrag 14:45 Uhr, Chemie HS3

gez. Professor Dr. Andreas Steffen

Gesellschaft Deutscher Chemiker

Ortsverband Dortmund