



ACS Local Section  
North Jersey

## Structural Determination of Neurodegenerative Disease-Associated Proteins Inside Cells

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**Date:** Thursday February 22nd, 2024

**Time:** 12:00 pm ET via Microsoft Teams

### Abstract

The misfolded proteins associated with neurodegenerative disease can adopt a variety of different conformations, some of which are toxic. Because these proteins have identical amino acid sequences, the cellular environment clearly influences the final state, yet most structural studies do not include the cellular context and, perhaps because we are not studying the correct conformation, not a single therapeutic strategy for these diseases addresses the underlying protein misfolding pathology. Using new sensitivity-enhancement technology for solid state NMR spectroscopy, Dynamic Nuclear Polarization, we study protein structure in native environments - inside living cells - to reveal how both healthy and disease-relevant cellular environments influence protein structure. Because NMR reports quantitatively, with atomic level precision, on all sampled conformation, it can not only report on structural polymorphs but also provide experimental restraints on regions of intrinsic disorder, complementing insights from cryo-electron microscopy and tomography. Using this approach, we recently demonstrated that an amyloid fibril with a solved cryo-EM structure was polymorphic and found that when those fibrils were used to seed amyloid propagation in mammalian cells, the minority polymorph in the purified setting became the majority polymorph inside cells. With this approach we can understand the mechanism of protein-based inheritance of amyloid aggregates and correlate phenotype with conformational ensembles.

### Connection Information

This will be a virtual meeting hosted via Microsoft Teams. A direct link to the meeting is located [HERE](#).

Further information can be found on the [NMR Topical Group website](#).

Please reach out to Christine Jorge ([christine.jorge@bms.com](mailto:christine.jorge@bms.com)) or Rongfeng Zheng ([rongfeng.zheng@bms.com](mailto:rongfeng.zheng@bms.com)) with any questions.

*Presented by the NMR Topical Group – North Jersey ACS*