

## Protein misfolding and aggregation in biomolecular condensates

We offer a 3 year PhD position that is jointly financed and supervised by Prof. Dr. Simon Ebbinghaus (Ruhr Universität Bochum, Germany) and Dr. Ralf Schweins (Institut Laue – Langevin (ILL) Grenoble, France).

Amyloid-associated pathologies commonly rely on non-native conformational transitions favored by factors like disease-related mutations, a decrease in solubility induced by cellular aging or stress, or failure of the protein quality control (PQC) mechanisms in the clearance of misfolded or aggregated species. Despite tremendous research efforts throughout the years to identify and inhibit the disease-relevant processes, the majority of the neurodegenerative diseases remain incurable. A significant advance in the field is now envisioned by considering phase separation as a crucial process in disease progression, since proteins involved in amyloid-associated pathologies, like TDP43 or FUS (Fused in sarcoma), play also a crucial role in phase separation. The aim of the PhD project is to unravel how biomolecular condensates modulate protein folding and aggregation pathways, leading to a novel understanding of condensate function in protein misfolding diseases.

Our experimental approach is based on complementary preliminary work in which fluorescence spectroscopy and microscopy was used to investigate the stability, aggregation and FUS condensate association of SOD1 (involved in ALS) under different in vitro and cellular conditions, leading e.g. to two previous publications (Gnutt et al., JACS 2019, Samanta et al., JACS 2021). During the 3 years of this project (1 financed by Ruhr University Bochum, 2 financed by ILL Grenoble), the PhD student will apply different scattering techniques to resolve the structural changes of the SOD1 monomer and the evolution of aggregate size in condensates. Molecular simulations (in collaboration with F. Sterpone (Paris) and S. Timr (Prague)) will be conducted to interpret the experimental data. The student will be further affiliated with network activities in the DFG Priority Program "Molecular Mechanisms of Functional Phase Separation" SPP2191 (<https://www.spp2191.com>).

The successful candidate will be enrolled at the doctoral school of the RUB. The project timeline is flexible to a certain extent. There will be an initial period of 1 year at RUB, followed by a stay at the ILL for the remaining 2 years of the contract. Short-time visits to the other partner are foreseen throughout the thesis, as well as regular video meetings.

We are seeking a highly motivated candidate with a background in biology, life sciences or soft condensed matter, and thus having a Master's degree in either biochemistry, chemistry or physics. A prior knowledge of scattering techniques (light scattering and/or small-angle scattering) as well as experience in molecular biology will be an asset. In order to analyse SANS data some basic programming skills (Python, Matlab, etc.) would be helpful.

For more information please contact Prof. Dr. S. Ebbinghaus ([s.ebbinghaus@tu-braunschweig.de](mailto:s.ebbinghaus@tu-braunschweig.de)) or Dr. R. Schweins ([schweins@ill.eu](mailto:schweins@ill.eu)). If you would like to apply for this position please send your documents to both supervisors.