Aggregation kinetics of amyloidic proteins

Supervisors / institute:
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Project background and description:

Protein misfolding diseases are fatal diseases including neurodegenerative diseases like Alzheimer's disease (AD), transmissible spongiform encephalopathies (TSEs) or Parkinson's disease (PD). In a continuously aging Western society, prevalence, socioeconomical and medical impact of these late-onset diseases increases. Therefore, a thorough understanding of the protein misfolding mechanism is essential, e.g. to establish reliable diagnostic methods and to find effective therapeutics.
Many of the described protein misfolding processes lead to formation of amyloid protein fibrils consisting of an array of alternatively folded proteins in a β-sheet rich structure. Prominent amyloidogenic proteins associated with neurodegenerative protein misfolding diseases are amyloid-β (AD), prion protein (TSEs) and α-synuclein (PD).
Within this project the mechanism of aggregate especially fibril formation will be analyzed on the single aggregate level. Due to the fact that different proteins form fibrils and are associated with neurodegenerative diseases, it is of major interest, if the aggregation mechanism e.g. kinetics is comparable or differs between these amyloidic proteins. Also the influence of different environments on the aggregation mechanism could give insights in molecular disease mechanism.
Compounds that interfere with the aggregation pathway from protein monomers to fibrils are considered to have drug potential. The mechanisms of ligand-fibril interactions and the influence of inhibitors on the polymerization kinetics of fibrils will deliver insights in possible therapeutically effects. Elucidation of these basic principles results in various applicative perspectives concerning diagnostics and therapy development as well as understanding of the molecular mechanism of neurodegenerative diseases.

Aims of the project:

- Elucidation of the aggregation mechanism e.g. kinetics of amyloidic proteins
- Comparison of different aggregation pathways
- Influence of potential therapeutics on protein aggregation

Requirements:

- Master degree in biology, biophysics, biochemistry or a related discipline in natural science
- Experience in fluorescence imaging, protein biochemistry, biophysical techniques, amyloid protein aggregation

Additional information:
http://www.uni-duesseldorf.de/MathNat/ipb/birkmann