Amyloid fibril formation near interfaces

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Amyloid-like fibrils and its precursors are associated with a number of severe diseases such as Alzheimer’s, Diabetes II or Chorea Huntington. Although the structure of the matured fibrils is well known, the detailed pathway from soluble, natively folded proteins to insoluble fibrils remains unknown. Furthermore it remains unclear which natural or artificial factors trigger the start of the aggregation process.

Our aim is to trace the pathway from oligomers to matured fibrils and to investigate the role of interfaces as a possible accelerator of the aggregation process. Therefore we combine the topological information obtained by Atomic force microscopy (AFM) with chemical information gained from thioflavin fluorescence and molecular dynamics simulations.

As model interfaces we investigate the influence of lipid bilayers, vesicles and nanoparticles of different sizes and different degrees of hydrophilicity on the fibril forming sequences of human islet polypeptide (hIAPP) and of yeast prion protein Sup35.

Initial experimental results indicate morphological changes and a narrowed thioflavin fluorescence spectrum for peptide (hIAPP) aggregation under the influence of lipid vesicles. This suggests an increasing excited state lifetime of the fibril formation sensitive fluorophor thioflavin.

With the help of fluorescence lifetime imaging (FLIM) it is possible to correlate morphological changes observed by AFM and the changes of the fluorescence signal temporally and spatially resolved.