Master thesis project, to be performed at Physical Chemistry, Department of Chemical and Biological Engineering, Chalmers University of Technology during 2011.
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Curing Alzheimers disease!?

Studies of interactions between amyloid aggregates and Luminescent conjugated polyelectrolytes to detect Alzheimer-causing pre-firbrillar states

Protein folding is a delicate process and what's usually are denoted as missfolding, where the polypeptide chains end up in a stable cross-beta fibrillar structure, randomly occurs. Enrichment of these fibrillar structures in tissue, in so called Amyloid plaques, is the pathologic hallmark of a large number of protein related diseases with Alzheimer's disease and Parkinson's disease being two of the most well known. The cause of missfolding is not fully understood and since this class of disease today is on the top five list of age related disease causing death, combined with an ageing population, there is a great demand of finding new ways of dissecting amyloid formation and protein missfolding.

Luminescent conjugated polyelectrolytes (LCPs) is a novel type of probes that have been shown to stain amyloid fibrils both *In vitro* and *In vivo and they are able* to discriminate between a number of different amyloid aggregate morphologies.[1] Additionally, contrary to conventional amyloid stains, including Thioflavin-T and Congo red, LCPs can detect both mature fibrils and pre-fibrillar aggregates.[2] Amyloid interaction is detected as a shift in the LCP fluorescence intensity or colour but the photophysics behind these shifts, including the type of interaction between LCPs and biomolecules, is not fully understood. Understanding these phenomena is crucial to improve the staining properties and the tantalizing idea of developing therapeutic compounds and assays.

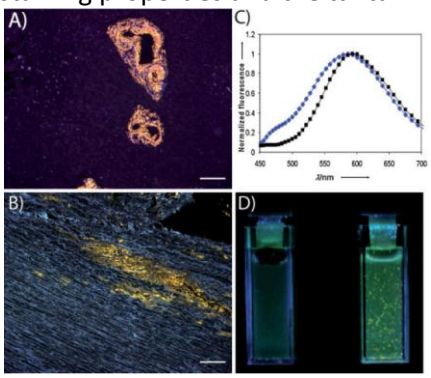

Figure A)–B) Fluorescence microscopy picture of amyloid plaques from two types of tissue, A) liver, B) muscle, stained with a cationic LCP, and corresponding fluorescence spectra C) black squares (A) blue diamonds (B).[4] D) Visual bacteria detection trough LCP staining, left mutated E.coli not expressing mannose receptors, right normal E.coli.[5]

In this project we mainly focus on comparing and examining interactions between LCPs and amyloids trough different types of spectroscopic methods and possibly matching distinct spectroscopic signals to LCP/amyloid conformations. One plausible method is flow linear dichroism,[3] which previously has been used to study interactions between dyes and elongated molecules, such as DNA. In flow-LD molecules are aligned in a sheer flow and the differences in absorption of linearly polarized light, parallel and perpendicular to the orientation axis, is measured. One of the benefits with flow-LD is that only the aligned and oriented molecules will contribute to the signal. Preliminary results show that the LCP are bound in an oriented fashion in between adjacent grooves running along the fibrillar axis.

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Referenser

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