



Contribution ID : 149

Type : **Poster**

Characterisation of model protein denaturation by SAXS

Thursday, 20 November 2014 17:30 (90)

The biological functions of proteins depend on the ability of the proteins to fold correctly. Misfolding/unfolding of proteins can cause formation of insoluble pathological aggregates, leading to degenerative diseases, such as Alzheimer's and Parkinson's [1]. Although considerable studies have been carried out on the molecular mechanism of protein aggregation, the lack of detailed information that links the initial stage of aggregation and the final structure limits the understanding of protein aggregation. In this study, our objective is to investigate the thermal denaturation and pre-aggregation of three soluble model proteins, ribonuclease A, myoglobin and chymotrypsinogen A, with different secondary structure characteristics. By using in situ small angle X-ray scattering, we can extract thermodynamic parameters and study the very early stages of the aggregation process-especially the conformational changes of individual protein molecules in solution on thermal denaturation. Our hypothesis is that the differences in aggregation mechanisms observed in the models proteins during thermal denaturation are intimately related to their secondary structures. These results will be complemented with chemical and high pressure denaturation to gain a complete thermodynamic picture of the different protein-types resistance to aggregation.

1. Tan, S. Y., & Pepys, M. B. (1994). Amyloidosis. *Histopathology*, 25 (5), 403-414.

Keywords or phrases (comma separated)

Protein aggregation, thermal denaturation

Summary

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Session Classification : Welcome Function, Poster Session, Exhibition

Track Classification : Structural Biology