A pipeline for time-resolved small-angle X-ray scattering data analysis on amyloid fibrils formation in solution

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Structural and functional biophysical studies often require temporal resolution to explore the kinetics of processes in macromolecular systems. The processes like amyloid fibrils formation and protein aggregation involve rapid consequent chemical reactions happening at native conditions [1]. Conformational changes caused by changing conditions have impact on the functionality of biological macromolecules and their complexes. Small-angle X-ray scattering (SAXS) is a structural method allowing one to capture conformational changes and measure kinetics of the macromolecules and complexes in near native solutions [2].

For functional biological complexes, it is important not only to observe structural changes, but also to recognise their biological implications with the help of additional information about the system. The sources if information can be e.g. an atomic model of a given state from cryo-electron microscopy or X-ray crystallography and/or simulated behaviour of the complex (molecular dynamics) under conditions of the time-resolved SAXS experiment [2, 3].

As the analysis of one dimensional SAXS data in terms of three-dimensional (3D) models is an ill-posed problem, and the analysis of kinetics needs the detection of time-dependent changes, characteristic times of the structural changes to need to be defined to analyse large amounts of time-resolved data. To do this, linear methods of reducing the dimensionality of data are being applied for obtaining time dependencies; statistical methods are utilised for the assessment of the importance of the contributing components and machine learning is used for data classification. The ATSAS software [4] is a powerful tool for small-angle scattering data analysis capable to extract rich structural information from the experimental data and also to fit the data with the available 3D models provided by other methods. This allows one to combine the structural information into a biophysical and biochemical evidence.

Although all the available ATSAS tools are straightforward to use, the data analysis still requires significant level of expertise to interactively utilize the tools when dealing with time-resolved studies. In order to optimise and simplify the data analysis procedures for the analysis of processes occurring in biomacromolecular systems, a new pipeline has been developed. The pipeline allows one to perform a comprehensive analysis and incorporates relevant components of ATSAS for the analysis of time-resolved. Its capacity is illustrated by the application to the time-resolved data on amyloid fibrils formation in solution.

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