Unravelling the speciation of β-amyloid peptides during the aggregation process by Taylor dispersion Analysis

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Gold statement
- Understand the challenges of amyloid Aβ peptide aggregation
- Reveal the analytical information that TDA can bring in the field of peptide/protein aggregation
- Assess the aggregation pathway of different Aβ peptides

Introduction
Peptide and protein aggregation are involved in many biological cellular mechanisms and diseases. The aggregation of beta-amyloid (Aβ) peptides and the formation of insoluble large aggregates are directly linked to the development of Alzheimer Disease [1]. Therefore, it is important to monitor the onset and the early stages of the aggregation. However, very few methods in the literature are able to do so. In this work, Taylor Dispersion Analysis (TDA) [2] is presented as a novel method capable to unravel the aggregation pathway and to shed more light on the formed species at each instant during the aggregation process.

Body
This communication aims at reporting the contribution of TDA for the study of peptide-peptide interactions by monitoring the aggregation process of Aβ(1-40) and Aβ(1-42). Indeed, TDA is a dispersion-based separation technique allowing to measure, by adequate data processing of the signal, the molecular diffusion coefficient and the hydrodynamic radius of each population present in the sample. In the present case, TDA allowed the monitoring of: (*i*) the consumption of the monomeric peptide and low molar mass oligomers, with information related to their size (R_h= 1.4 – 2.0 nm), (*ii*) the transient appearance (quantity and average size) of oligomeric species (R_h= 3 – 30 nm), and (*iii*) later on, the formation of protofibrils (R_h >50 nm) before (*iv*) the precipitation of large fibrils. These results were obtained by applying two different data treatment methods and were correlated with the well-known ThT fluorescence assay, usually used for evaluating the kinetics of the fibril formation. To our knowledge, no other technique is able to deliver such information regarding the complete speciation of the Aβ peptides, and in our opinion will bring new insights to the field. The results were consistent with the amyloid hypothesis and will be thoroughly discussed during the talk.

Conclusion
TDA is a valuable method able to size under physiological conditions over a wide size range (1 nm to ~200 nm) and to unravel the Aβ peptide speciation, shedding the light on the early stages of the aggregation process of Aβ peptides.

References
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