Aβ peptides and β-sheet breakers. A coarse grained molecular dynamics approach using GO-Martini

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The problem of protein misfolding is at the origin of a class of pathologies called protein conformational disorders (PCD) to which all neuro-degenerative diseases belong. PCD's are characterized by the misfolding of proteins that grow in aggregates of fibrillar shape. Among them, Alzheimer Disease (AD) is one of the most studied for its high impact on the modern society. The plaques present in the brain of AD patients show deposition of fibril made of amyloid β (Aβ) peptides [1]. The process that leads to misfolding, aggregation and amyloid plaques formation is not yet fully elucidated. It seems, however, that the "trigger" of the process is an abnormal switch of the peptide secondary structure leading to β-sheet formation.

Nowadays an effective treatment for AD is still missing. Several factors are known to affect Aβ aggregation processes. An important role seems to be played by metal ions that have been observed to be quite abundant in fibrils [2-4]. Recent observation of short synthetic peptides, called β-sheet breaker (BSB's), are able to directly interact with Aβ, precluding (or disfavoring) amyloid polymerization. This finding has stimulated a lot of work in the direction of trying to understand the molecular mechanism by which BSB's are able to slow down or even prevent Aβ aggregation and fibrillation processes. [5].

In this presentation we show how one can get a good understanding of the role that BSBs play in the aggregation process of Aβ peptides by means of *coarse-grained molecular dynamics* simulations based on the Martini force-field. Since the secondary structure switching is a crucial event for the successive aggregation process, we have extended the standard Martini approach to incorporate GO-Martini algorithm [6] that allows to properly model structural switches and to study the secondary structure dynamical evolution of Aβ peptides in the presence of BSBs.

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