O-20.4 Short talk

Metal Ions in Amyloid-β Misfolding and Aggregation: an X-ray Journey from Static Structures to Dynamic Processes

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The accumulation of misfolded amyloid- β (A β) peptides in oligomeric and fibrillar forms is a hallmark, and one of the possible pathogenetic mechanisms, of Alzheimer's disease. The presence of metal ions, in particular Cu, Zn, and Fe, is a relevant factor influencing the misfolding and aggregation process. In particular, Cu ions bound to the A β peptides represent a source of oxidative stress because of their redox activity.

Here, the application a combined X-ray Absorption Spectroscopy (XAS) and molecular dynamics approach to probe the local coordination environment and oxidation states of metal ions bound to $A\beta$ is presented. Synchrotron XAS experimental results on Cu(I), Cu(II) and Zn(II) ions in complex with the 1-6 and 1-16 fragments of the $A\beta$ peptide are presented. The effect of the interaction with the X-ray beam on the metal oxidation states and on the peptide structure in the presence of the two different metals and under different temperature and X-ray irradiation conditions is analysed.

Finally, the possibility of performing combined XAS and fiber diffraction measurements at Free Electron Laser radiation sources to gain insight into the dynamics of metal-A β complexes and to clarify the interactions between metal ions and A β fibrillar aggregates is discussed.