Amyloid β peptide in complex with Cu(II) ions and beta-sheet breaker peptidess

X-ray absorption Spectroscopy experiments were performed at the ESRF beamline BM30B to study the effects of two different beta-sheet breaker peptides (BSBs) on the Cu(II) and Zn(II) coordination mode with the amyloid β (Aβ) peptide $A\beta_{1\text{-}40}$, which is involved in Alzheimer's disease pathogenesis.

The amino acid sequences of the two BSBs are LPFFD (for short ASP) and LPFFN (for short ASN). Aβ concentration was 0.66 mM in all the measurements. Cu(II) and Zn(II) concentrations are taken to be sub-stoichiometric, 0.53 mM, while ASP and ASN are both over-stoichiometric, 3.3 mM.

Sample	[Aβ - Peptide] mM	[Cu] mM	[ASP] mM	[ASN] mM
CuB	0	2.11	0	0
CuS	0.66	0.53	0	0
CuI6	0.66	0.53	0	3.3
CuI12	0.66	0.53	3.3	0
CuC6	0	0.53	0	3.3
CuC12	0	0.53	3.3	0

Table 1. Each sample is identified by a four letters code, CuXn. X identifies the sample with the following acronyms: B, buffer (4-Ethylmorpholine); S, Ab alone; I, Aβ + BSBs; C, BSBs alone n, identifies the BSB present in solution namely 6 for ASN and 12 for ASP

As seen in Fig. 1, the XANES of all the systems are significantly different from that of the buffer, meaning that Cu is always bound to Aβ or BSB's when present. Qualitatively one can notice that CuS is very similar to CuI6 (Aβ + ASN) and significantly different from CuI12 (Aβ + ASP) thus suggesting that ASP affects Cu-Aβ binding while ASN does not.

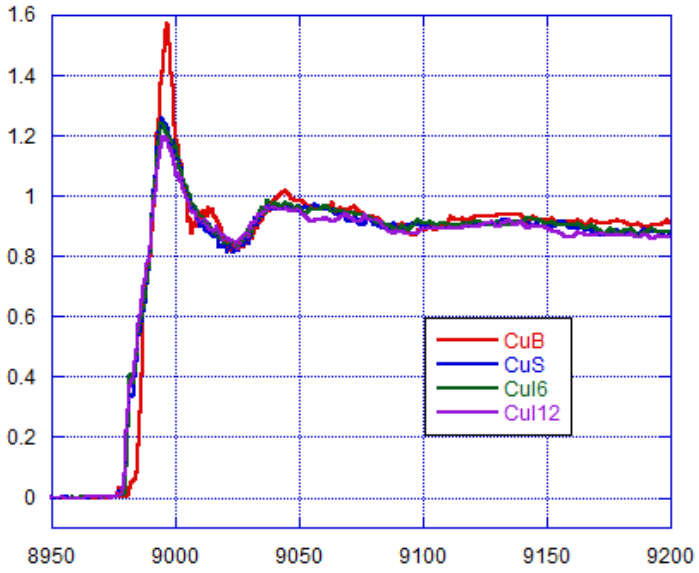

Figure 1

Analysing the experimental data we could then show that, at the low temperatures employed in XAS experiments, the time needed for collecting a good quality XAS spectrum is significantly shorter than the time after which structural damage becomes appreciable. Looking at the XAS peak in the pre-edge region associated to the transition of Cu from the oxidized to the reduced form under ionizing radiation, we showed that there exists a sufficiently large time window in which good XAS spectra can be acquired before the structure around the oxidized Cu(II) ion reorganizes itself into the reduced Cu(I) ‘‘resting’’ structure [Stellato 2019].

References

Stellato, F., Chiaraluce, R., Consalvi, V., De Santis, E., La Penna, G., Proux, O., ... & Morante, S. (2019). Dealing with Cu reduction in X-ray absorption spectroscopy experiments. *Metallomics*, *11*(8), 1401-1410.