ESRF	**Experiment title:** Competing influence of Interfaces and Transition Metal Ions on the Conformation of Amyloidogenic Model Peptides	**Experiment number:** SC-3036
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Report:

There is an intense debate if binding of metal ions to peptides may be responsible for serious diseases like Alzheimer's disease. Therefore, this study investigates the competitive binding of Cu^{2+} and Zn^{2+} with model peptides at the hydrophobic-hydrophilic interface.
The model peptides used in this study are de novo designed to exhibit concentration and time dependent amyloid formation. Besides the possibility for nonspecific complexation, the peptides carry specific metal ion binding sites (histidine residues, His) in different geometries. The His binding sites are located in the residue i and four amino acids further for the peptide i,i+4 and in position i and i+2 for the peptide i,i+2 respectively.
In bulk and at the air-water-interface, the peptides respond to the addition of Zn^{2+} and Cu^{2+} in different ways. This result raises the need of quantification for the metal ion binding to the peptide confined to the interface.
The peptide surface layers are highly suitable for total reflection X-ray fluorescence characterization at ID10B because only metal ions that are complexed to the peptide specifically are excited and detected.

In competition experiments, a preference for Cu^{2+} being bound to the surface with the peptide could be observed. It is reasonable to presume that it has additional binding sites, probably at the N-Terminus of the peptides.
The relative amounts of bound metal ion per area at a surface pressure of 25 mN/m are obtained by integration and normalization of the signals in the fluorescence spectra. When Cu^{2+} and Zn^{2+} are present at the same time, the amount of Zn bound to the peptide at to the hydrophobic-hydrophilic interface is very low with respect to a layer where the peptides are complexed with Zn^{2+} only. This indicates that Cu^{2+} does not only occupy additional binding sites. Also, the affinity of His binding sites is larger for Cu^{2+} than for Zn^{2+}. The binding constants of Cu^{2+} and Zn^{2+} to His in bulk follow the same tendency.
Interestingly, not only the amount of Zn is decreased for i,i+4, but also the amount of Cu per area decreases when both metal ions are present at the same time. Changes in Cu^{2+} affinity because of simultaneous Zn^{2+} complexation that can alter local conformations or changes on packing density have to be taken into account. Unfortunately, they are not experimentally accessible.

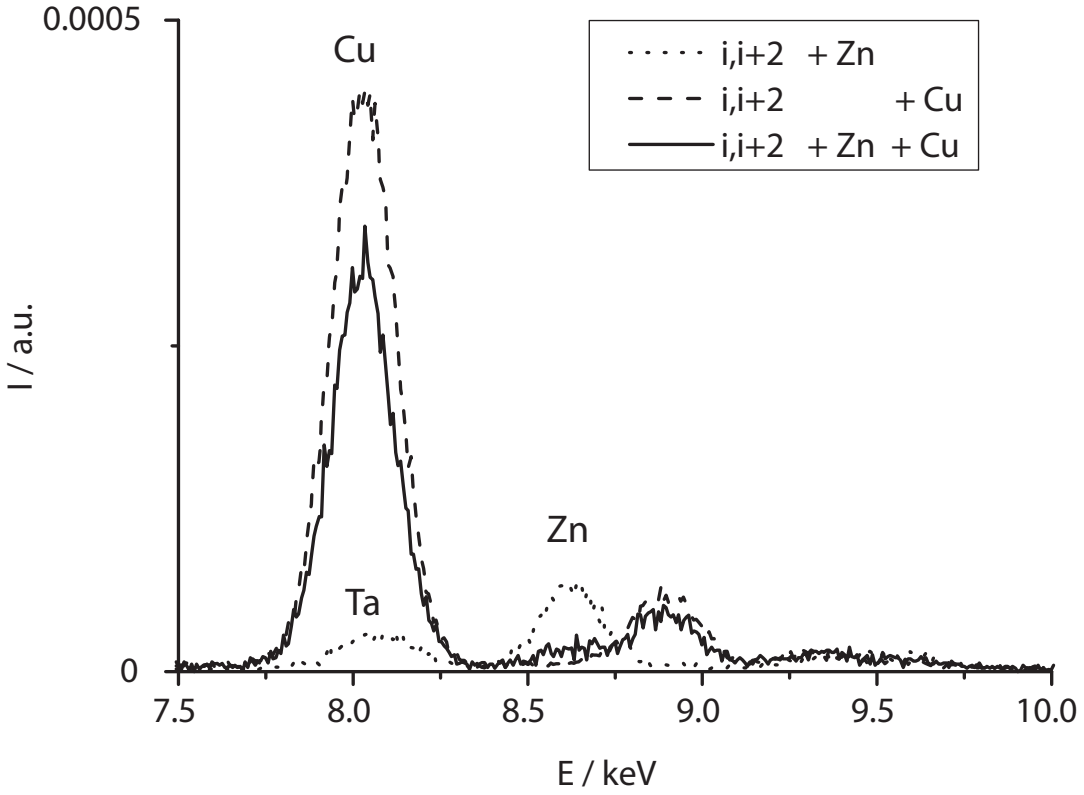

Figure 1.: X-ray Fluorescence spectra of i,i+2 at the air-water-interface (25 mN/m 0.3 μM in bulk, 10 mM PBS, pH 7.4 150 mM NaCl; Metal ions 2 μM for experiments using one metal ion, 2 μM Zn^{2+} and 2 μM Cu^{2+} in competition experiments)