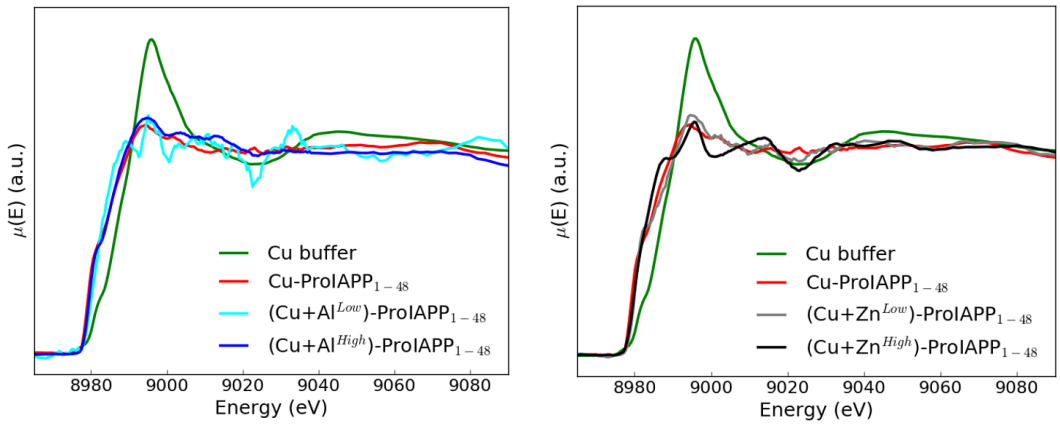
X-Ray Absorption Spectroscopy Measurements of Cu-ProIAPP Complexes at Physiological Concentrations

The amyloidogenic islet amyloid polypeptide (IAPP) and the associated pro-peptide ProIAPP$_{1\text{-}48}$ are involved in cell death in type 2 diabetes mellitus. It has been observed that interactions of this peptide with metal ions have an impact on the cytotoxicity of the peptides and on their deposition in the form of amyloid fibrils. We performed X-ray Absorption Spectroscopy (XAS) measurements of Cu(II)-ProIAPP complexes in physiological (10 µM), with equimolar concentrations of Cu(II) and peptide. Such low concentrations were made accessible to XAS measurements owing to the use of the High Energy Resolved Fluorescence Detection XAS facility recently installed at the ESRF beamline BM16 (FAME-UHD). Our data show that XAS measurements at micromolar concentrations are feasible and confirm that ProIAPP$_{1–48}$-Cu(II) binding at near-physiological conditions can be detected [De Santis 2019].



(**A**) (**B**)

Figure 1. The XANES spectra of the Cu-buffer (green line) and Cu-ProIAPP$_{1–48}$ sample in the absence of metal ions (red line) compared in panel (**A**) with the Cu-ProIAPP$_{1–48}$ spectrum in the presence of 50 µM Al(III) (light blue line) and 1500 µM Al(III) (blue line) and in panel (**B**) in the presence of 50 µM Zn(II) (grey line) and 1500 µM Zn(II) (black line).

The XANES spectrum of Cu in buffer displays features typical of hydrated copper, while the XANES spectrum of Cu-ProIAPP$_{1–48}$ has a different shape, indicating that Cu is bound to ProIAPP$_{1–48}$. Zn(II) and Al(III) added in solution seem to affect the Cu-ProIAPP$_{1–48}$ coordination mode in a way that depends on their concentration.

References

De Santis, E., Shardlow, E., Stellato, F., Proux, O., Rossi, G., Exley, C., & Morante, S. (2019). X-Ray absorption spectroscopy measurements of Cu-ProIAPP complexes at physiological concentrations. *Condensed Matter*, *4*(1), 13.