



	Experiment title: NiSOD mimics based on peptide-like ligands. A XAS study to correlate activity to the active site structure.	Experiment number: <u>30-02 1132</u>
Beamline: BM30	Date of experiment: from: 22/11/2017 to: 28/11/2017	Date of report: 14/02/2018
Shifts: 15	Local contact(s): Olivier Proux	<i>Received at ESRF:</i>
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Report:

Objective of the experiment:

This experiment aimed at proving the coordination sphere of the Ni ion by XAS in complexes that mimic the active site of the NiSOD, an enzyme that protects cells from the radical anion $O_2^{\bullet-}$.^{1,2,3} These complexes, developed by J. Domergue as part of his PhD project, are based on peptide-like ligands in order to obtain efficient catalysts for superoxide dismutation and to contribute to the understanding of the catalytic mechanism of the NiSOD. To reach this goal, it is necessary to determine precisely the coordination sphere of the different complexes in order to establish a structure/reactivity relationship.

Results:

Ni K-edge XAS spectra were acquired for 18 different samples at low temperature (10 K): reference nickel complexes in solid state with known structures, and four nickel complexes developed in the laboratory with cysteine and histidine based pseudo-peptide ligands, which coordination was studied at different pH. XAS data acquired with two catalytically active complexes are detailed here after.

First of all, the XANES spectra evidence that all of our complexes have a square planar geometry like in the enzyme, as both the $1s \rightarrow 4p$ and $1s \rightarrow 3d$ transitions can be seen in the pre-edge region.⁴

Preliminary results have shown that the complex NiL undergoes a deprotonation at pH 9 to promote an amidate coordination in NiLH₋₁ and the departure of a water molecule. The difference between the two species is clearly visible in the XANES spectra where the $1s \rightarrow 4p$ transition is more intense at higher pH. As expected from DFT calculations, EXAFS spectra are very similar since the replacement of an oxygen atom by a nitrogen atom does not have a significant effect. In both cases, the data are correctly interpreted with three S at 2.22 Å and a lighter atom (N or O) at 2.02 Å (Figure 1).

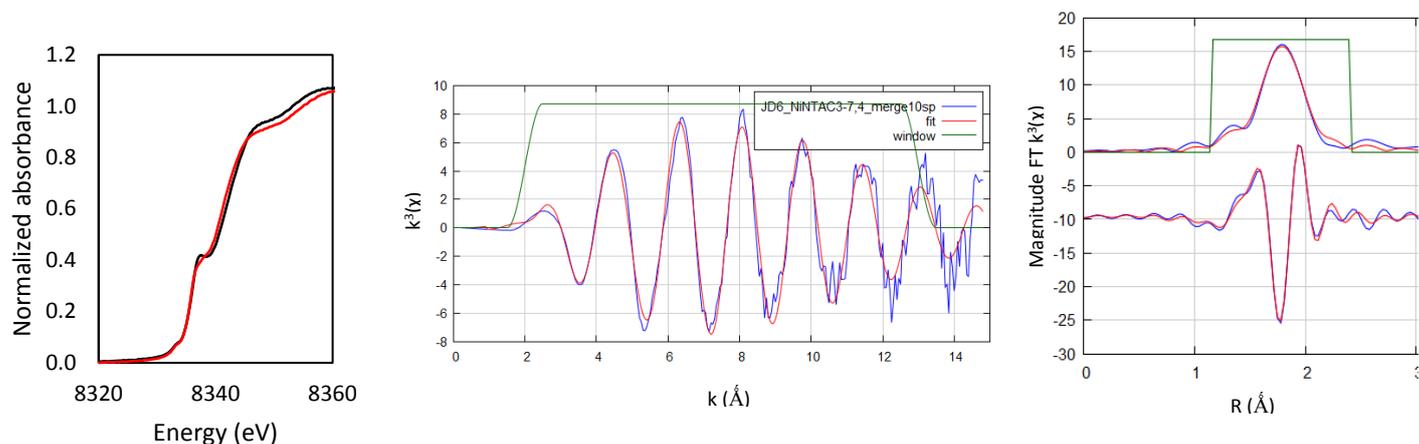


Figure 1: (left) XANES Spectra of NiL at pH 7.5 (red) and NiLH₁ at pH 9.6 (black); (middle) k^3 EXAFS spectrum, (right) modulus and imaginary parts of the Fourier transformed k^3 spectrum (blue) and the simulations (red) for NiL at pH 7.5. Simulation parameters: $\Delta E_0 = 3.4$, $s^2 = 0.87$, shell no. 1: Ni-S, $n = 3$, $r = 2.22 \text{ \AA}$, $\sigma^2 = 0.00296 \text{ \AA}^2$; shell no. 2: Ni-O, $n = 1$, $r = 2.02 \text{ \AA}$, $\sigma^2 = 0.00050 \text{ \AA}^2$; $R = 0.52\%$.

The 2nd most interesting Ni(II) complex regarding SOD-like activity is likely to form two coordinations, either N2S2 or N3S. The first analysis of the EXAFS data tend to confirm the second possibility but will be refined during the following months (Figure 2). However, supplementary analysis with derivatives are needed to determine exactly the coordination sphere around the nickel ion.

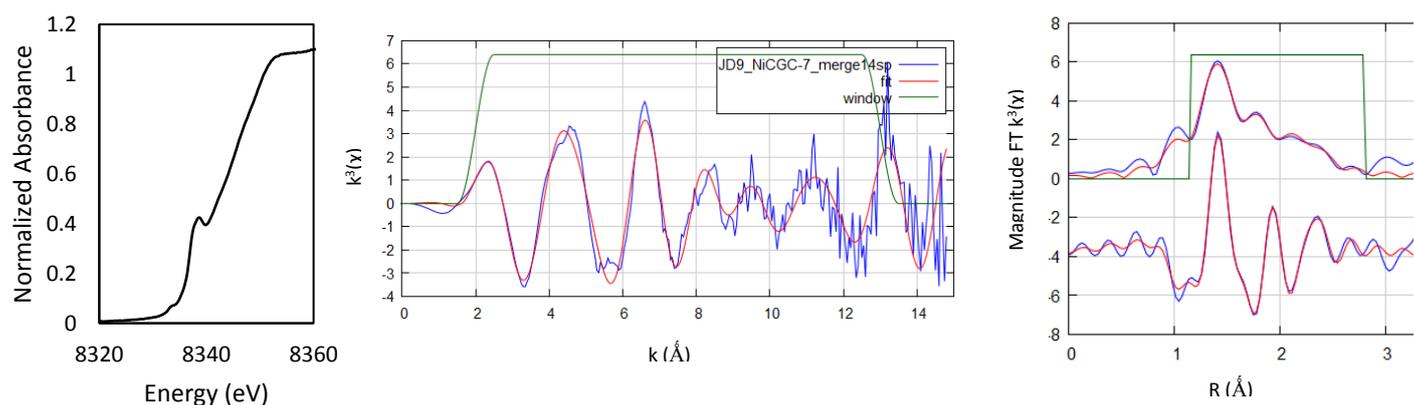


Figure 2: (left) XANES spectrum of NiP at pH 7.2, (middle) k^3 EXAFS spectrum, (right) modulus and imaginary parts of the Fourier transformed k^3 spectrum (blue) and the simulations (red) for NiP at pH 7.2. Simulation parameters: $\Delta E_0 = -2.89$, $s^2 = 0.87$, shell no. 1: Ni-N, $n = 2$, $r = 1.87 \text{ \AA}$, $\sigma^2 = 0.00186 \text{ \AA}^2$; shell no. 2: Ni-N, $n = 1$, $r = 2.09 \text{ \AA}$, $\sigma^2 = 0.00186 \text{ \AA}^2$; shell no. 3: Ni-S, $n = 1$, $r = 2.15 \text{ \AA}$, $\sigma^2 = 0.00243 \text{ \AA}^2$; shell no. 4: Ni-C, $n = 6$, $r = 2.90 \text{ \AA}$, $\sigma^2 = 0.03305 \text{ \AA}^2$; $R = 3.32\%$

Conclusion:

Thanks to these experiments, we were able to obtain crucial informations on the nickel environment in our different complexes. First of all, our tripodal ligands allow us to obtain a square planar geometry around the nickel and to get close to the enzyme's active site. Secondary, the XAS data confirmed the behaviour of the complexes with pH. Finally, EXAFS data are currently being refined in order to determine precisely the coordination spheres around nickel in all the complexes in order to define a structure/reactivity relationship. Supplementary analysis with NiP derivatives are however needed to determine exactly the coordination sphere around the nickel ion in this SOD active complex.

References:

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