ESRF	**Experiment title:** X-ray absorption studies of adducts of gold and ruthenium anticancer metallodrugs with serum proteins and fragments of proteins	**Experiment number**: 08-01 802
Beamline:	**Date of experiment**: from: 24/02/2008 to: 27/02/2008	**Date of report**: 11/03/09
Shifts:	**Local contact(s)**:Dr. Chiara MAURIZIO	*Received at ESRF:*

Names and affiliations of applicants (* indicates experimentalists):

ISABELLA ASCONE

CHIARA MARCHIONI

ANTONELLA BALERNA

CHIARA GABBIANI

Report:

The mechanisms through which metal complexes exert their biological and pharmacological effects are still largely unexplored. In particular various gold(III) and gold(I) compounds were shown to be very active *in vitro* against several human tumor cell lines. However the mechanisms leading to the relevant cytotoxic effects have not been elucidated yet. It seems that the direct interaction of gold compounds with a variety of protein targets may be particularly relevant. This research project was specifically directed to model the interaction of various gold compounds with some typical protiens.

We performed at GILDA beam line, EXAFS/XANES investigations aimed at characterising, at a molecular level, the adducts that are formed in the reaction of representative metallodrugs (Auxo6, Auranofin, AuL13, Aubipy) with selected proteins: bovine serum albumin (BSA) and Apotransferrin (TF).

We performed our experiments at Au L_3-edge 11.92 keV to obtain information on redox state of metals bonded to proteins and to define structural details on metal sites in protein.

The quality of EXAFS and XANES experimental data was good allowing a reliable simulation of spectra. Figures 1 show XANES spectra of metallodrugs and of metallodrugs/proteins adducts. In Fig. 2, the EXAFS spectra of Auoxo6 metallodrug and Auoxo6 metallodrug/Auoxo6Tf and their fit are shown.

For Aubipy XANES have been simulated in the frame of non muffin-tin approximation with a good agreement between experimental data and theoretical spectra. The optimized geometries for Au-bipy were calculated by the all-electron density functional theory (DFT) approach implemented[1] in the ADF2008 code. The self-consistent field simulation of Au-bipy is presented in the figure 3 (Soldatov et al. manuscript in preparation).

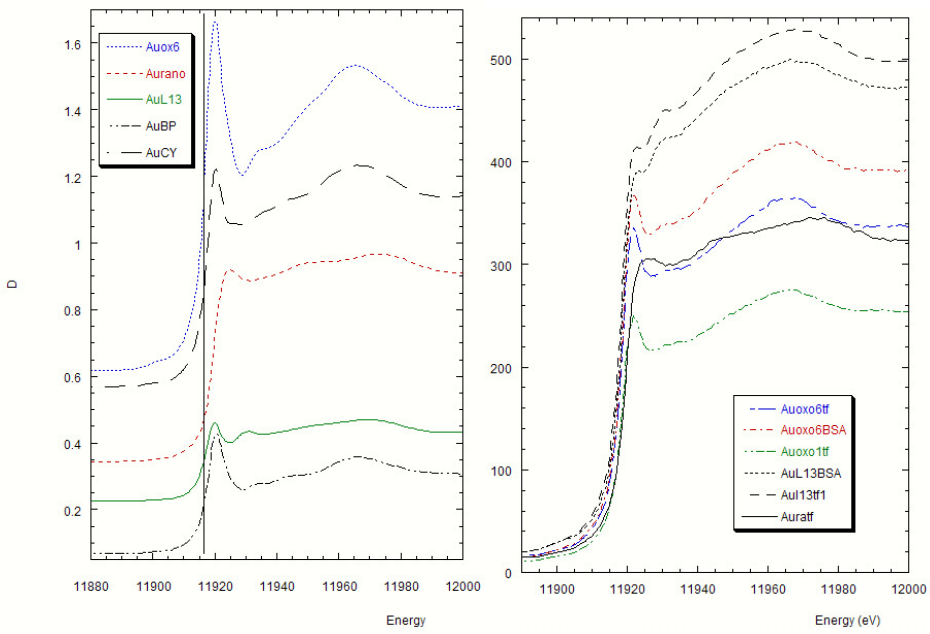
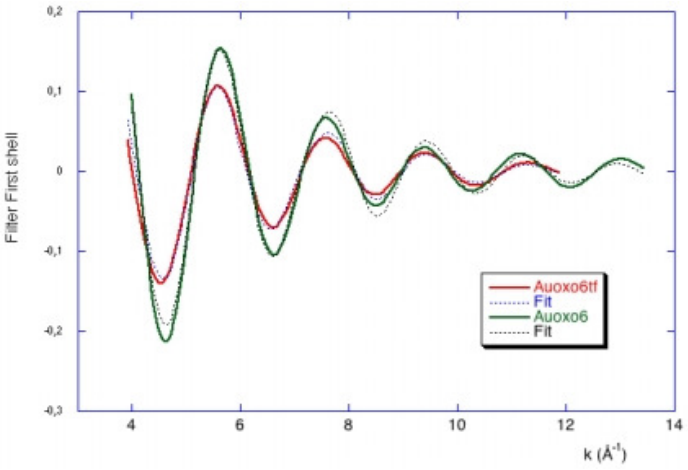


Fig 1 . A Fig. B



In Fig. 2 the EXAFS spectra of Auoxo6 metallodrug and Auoxo6 metallodrug/Auoxo6Tf and their fit are shown

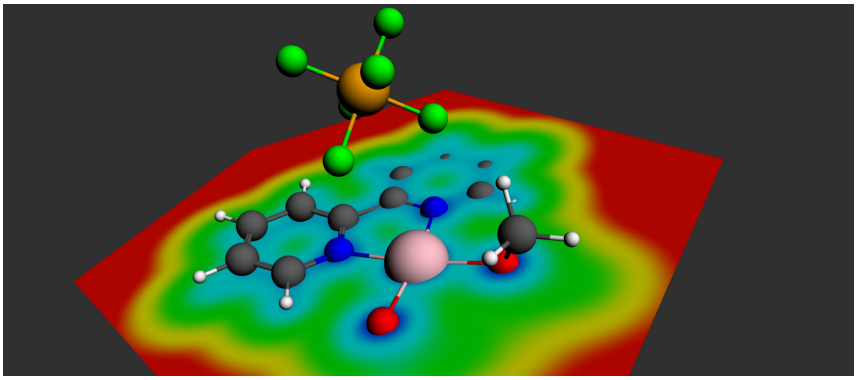


Fig.3 Results of the DFT SCF simulations of Au-bipy.