EUROPEAN SYNCHROTRON RADIATION FACILITY
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Experiment Report Form

ESRF	**Experiment title:** Human ferritin shape variation as a function of metal content: a correlation with pathology.	**Experiment number**: **MX-1022**
Beamline: ID14 3	**Date of experiment**: from: 09 apr 2010 to: 12 apr 2010	**Date of report**:
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Report:

Increased iron concentration in tissues appears to be one of the major factors in the development of several inflammatory and degenerative diseases; in particular, elevated iron concentrations in brain tissue seem to be involved in some neurological diseases, such as Alzheimer's disease (AD). Many experimental findings suggest that Fe accumulation in brain could be strongly linked to the presence of ferritin dysfunctions. As, indeed, recently demonstrated, ferritin iron core composition differs between physiological and AD's brain ferritins, where an increase of toxic ferrous iron (Fe^{2+}) has been detected [1]. In this context, providing a clear understanding of the mechanism behind the release of toxic Fe^{2+} from ferritin core may help to elucidate the role of ferritin dysfunctions into the development of neurological disorders [2].

In this experiment, Small angle X-ray scattering has been used to study the toxic Fe^{2+} release from ferritin. Iron release has been induced by means of chemical reduction using sodium dithionite. The structure of ferritin core as a function of its metal content has been studied during the iron release process.

In fig. 1 we show the scattering curves as a function of time, during the iron release process. In the insets of fig. 1 we show a detail of the scattering curves in the range 0.5-1 nm^{-1} (on the right) and the dependence of the I versus q intercept at q=0 (on the left). As expected, the intercept at q=0 decreases with time. This trend indicates that the molecular mass of the protein is decreasing [3] as a consequence of the iron release from the ferritin cavity.

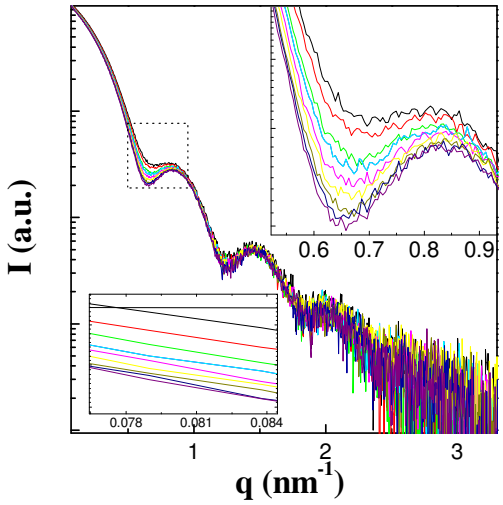

Fig. 1 scattering curves as a function of time, during the iron release process

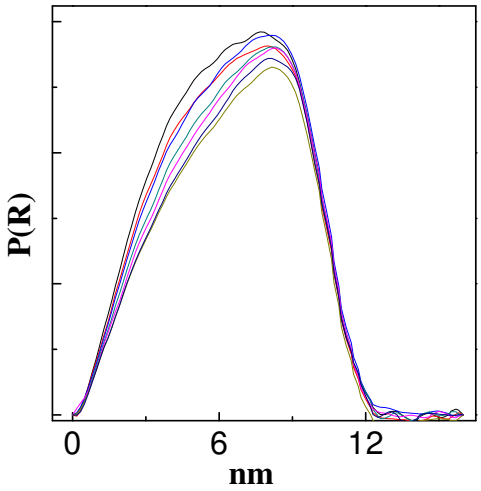

Fig. 2 Pair distribution function as a function of time.

The scattering curves have been analysed in terms of pair distribution functions (PDF), usign the regularized inversion program GNOM [4]. The result reflects the characteristic PDF changes upon iron release. As the ferritin metal content decreses, it can be observed a systematic reduction of the contribution of PDF signal at 4 nm.

To obtain a deeper understanding of the structural features of the ferritin core during the iron release process, the I(q) curves have been analyzed by means of the program Dammin [5]. The complete analysis will be presented elsewhere. In summary, our analysis allowed us to measure the density variations of the ferritin core as a function of time and distance from the core centre i.e. to provide reliable time-resolved three dimensional model of the core during the iron release process. Furthermore we observed that the iron release process proceeds towards several steps, namely a defect nucleation in the outer part of the mineral core, the diffusion of the reducing agent towards that inner part of the core and, finally, the erosion of the core from its inner to the outer part.

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