

## Near-Edge Absorption Soft X-ray Nanotomography of Cells Incubated with Nanoparticles

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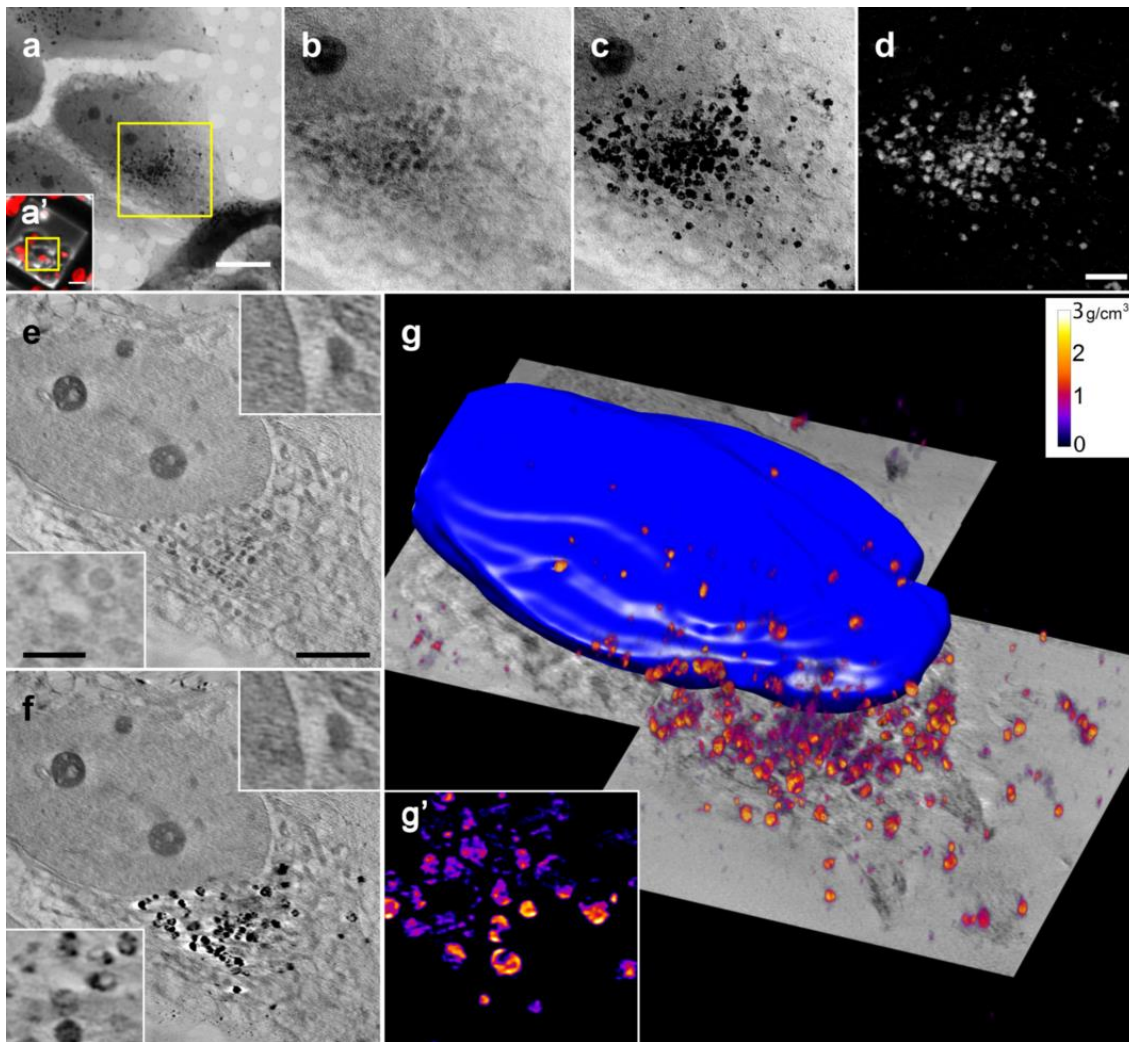
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Superparamagnetic iron oxide nanoparticles (SPION) have become important tools in nano-biotechnology and nano-biomedicine. These new developments require a precise quantitative analysis at sufficient spatial resolution to model the interactions between nanoparticles and the cellular structures in a quantitative way. The results from this analysis will determine the dose for either drug-delivery or hyperthermia treatments as well as its feasibility. To tackle this issue 15 nm dimercaptosuccinic acid functionalized SPION were incubated with MCF-7 breast cancer cells [1] as a model system to be analyzed exploiting the iron differential absorption contrast at the L3 iron edge. Near-edge absorption soft X-ray nanotomography (NEASXT) combines whole-cell 3D structure determination at 50 nm resolution, with 3D elemental distribution and quantification and high throughput. We have solved the three-dimensional distribution and quantification of SPIONs within the cells with sufficient sensitivity to detect the density corresponding to a single nanoparticle in the whole cellular volume (Fig. 1) [2].

### References:

[1] M. Chiappi, J.J Conesa, E. Pereiro, *J Nanobiotechnology* **14**(1) (2016), p. 3.

[2] J.J Conesa, J. Otón, M. Chiappi, *Scientific Reports* **6** (2016), Article number: 22354.



**Figure 1.** Correlative microscopy, differential tilt-series generation and 3D representation. **a)** Soft X-ray projection images mosaic (709 eV) of MCF-7 cell incubated with iron nanoparticles. Scale bar 25  $\mu\text{m}$ . Inset in **a')** *In vivo* fluorescent image of the same cell. Acidic organelles are labeled with Lysotracker (red). Scale bar, 20  $\mu\text{m}$ . **b)** and **c)** X-ray projection images at 700 and 709 eV respectively. Scale bar, 2  $\mu\text{m}$ . **d)** Difference image generated combining images at 700 and 709 eV. Scale bar, 2  $\mu\text{m}$ . **e)** and **f)** Central slice of reconstructed tomograms at 700 and 709 eV respectively. Scale bar, 2  $\mu\text{m}$ . **g)** Volumetric representation of iron oxide densities within the cells, forming clusters near the nucleus.