Correlative 3D structural and chemical quantification of single human cells

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X-ray microscopy is increasingly used in biology, but in most cases only in a qualitative way. We present here a correlative X-ray microscopy approach suited for quantification of molar concentrations in cells at nanometre scale. By combining the elemental content provided by X-ray fluorescence microscopy and the morphology information extracted from X-ray phase nano-tomography, we determine the intracellular molarity distributions. This method was first demonstrated on a freeze-dried human macrophage cell to obtain the absolute elemental concentration maps of biologically relevant elements (Figure 1) [1]. The cell morphology results showed a very good agreement with atomic-force microscopy measurements. The correlative approach was extended to three dimensions and to the quantification in terms of local mass fractions on malaria-infected red blood cells [2]. While these proofs of principle were performed on freeze-dried cells, we pushed further the technique to cryo-preserved cells to better safeguard the cellular structure and elemental content. The quantification of major and minor elements, as well as the density, were extracted in the different organelles of frozen-hydrated cells. This work opens the way for in-situ single cell structural and chemical analysis down to sub-organelle level using exclusively synchrotron radiation techniques.

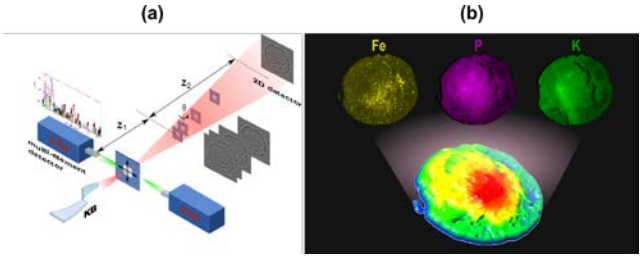

Figure 1: a) Acquisition scheme of correlative X-ray fluorescence and X-ray phase contrast imaging b) Bottom: macrophage cell thickness derived from X-ray phase contrast nano-tomography. Top: elemental concentrations in the cell derived by the correlative method.

References

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