Imaging of Intracellular Metal Distribution by X-ray Microfluorescence

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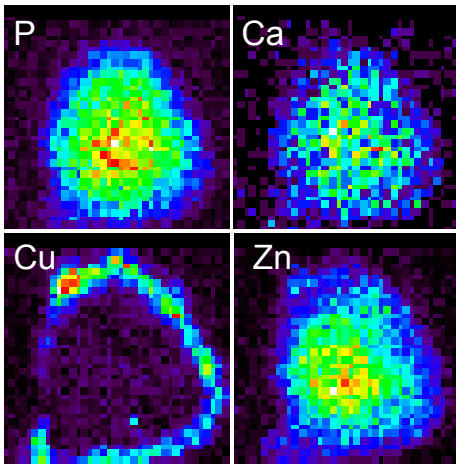
X-ray fluorescence microscopy is ideally suited for studying trace metal distribution due to its inherent elemental sensitivity of better than part-per-million. It enables studies of inter- and intra-cellular distributions of elements from P to Zn and above, with simple yet accurate quantification. Because a finely focused x-ray beam is used to excite the atomic emission, the total metal concentration is measured directly without the need of labeling with fluorescent sensors. This provides a complementary technique to conventional optical fluorescence microscopy which mainly detects chelatable metals. A spatial resolution of ~ 200 nm is achieved routinely, with the minimum detection limit as low as 3 attograms ($3x10^{-18}$ gm) for zinc within one second of data acquisition time. As illustrated in the figure, typically several elemental maps (up to ~15) were acquired simultaneously, thus ensuring complete alignment between the images. The large penetration depth of x-ray allows the study of whole cells without sectioning, tissue sections of > 10 μm thickness, and hydrated/frozen samples. In addition, the possibility of performing micro-XANES analysis at discrete locations enables the oxidation state for the element of interest to be determined. These unique capabilities had been employed in single cells and bacteria studies of environmental toxins (As, Hg, Pb, U), carcinogens (Cr), therapeutic agents (Pt, Sb), nanobiocomposites (Ti), and metalloproteins (Fe, Cu, Zn). We will discuss instrumentation and methods that have been implemented, demonstrate their application in ongoing studies, and delineate the future prospects.



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