SIMS Applications to Medical Research: Radiation Protection

Intracellular uranium detection

Uranium is a radioactive metal that humans can be exposed to as a result of its natural presence or occupational activities such as mill tailings, nuclear industry or military use. The mechanisms of uranium toxicity have not been fully elucidated, especially at low concentrations in cell compartments. Localization of uranium within cells is therefore mandatory for the comprehension of its cellular mechanism of toxicity.

Microdistribution of uranium within the cells

Secondary Ion Mass Spectrometry (SIMS) has proven useful in life sciences to study biological samples, in particular to detect and localize uranium at very low concentration levels within cells. It has been shown by SIMS that, at low noncytotoxic concentration, soluble or precipitate forms of depleted uranium inside the cells play a role in biological cell response. Moreover, SIMS results have shown for the first time the presence of soluble uranium within the nuclei after 15 min to 24 hours of exposure to concentrations lower than 100 µM (Figure 1).

Comparison of cryogenic versus chemical sample preparation methods

The SIMS technique requires specific sample preparation, achieved by implementing different chemical treatments to preserve as much as possible the native uranium distribution in the analyzed sample. A recent study compares the bioaccumulation sites of uranium within liver or kidney cells after chemical fixation or cryomethod preparation of the samples (Figure 2). The direct comparison of chemical or cryogenic preparation using different cell types confirmed the presence of uranium within the cell nuclei and showed that this distribution is only slightly altered by the sample preparation process.

Excellent detection limits using SIMS

Using the IMS 7f-GEO, mapping of major and trace species can be obtained at cell level in biological samples with a lateral resolution reaching ~0.5 µm. Other strengths of the instrument include its versatility (mass spectra, depth profiling analysis, etc.), high throughput, as well its high sensitivity resulting in low detection limits for several elements of interest including heavy metals such as uranium.

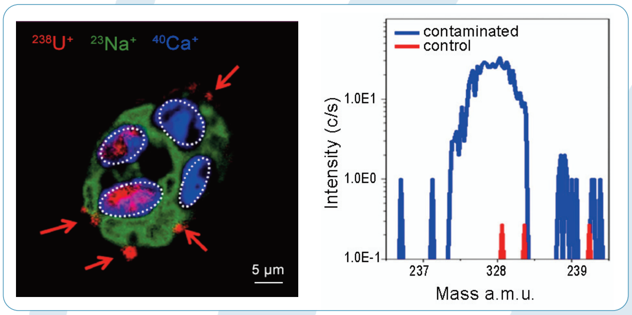

Figure 1: Uranium distribution inside the HepG2 cells in soluble and precipitate forms after exposure to 100 µM of uranyl nitrate for 30 min. Superposition of $^{238}U^+$, $^{23}Na^+$ and $^{40}Ca^+$ SIMS ion images and ^{238}U mass spectra. Red arrows indicate ^{238}U precipitates. White circles delimit the nucleus. Field of view: 50 x 50 µm².

Data collected on IMS 7f at IRSN Fontenay-aux-Roses (France). Adapted from Y. Guéguen et al., Toxicology in Vitro (2015) DOI: 10.1016/j.tiv.2015.09.004.

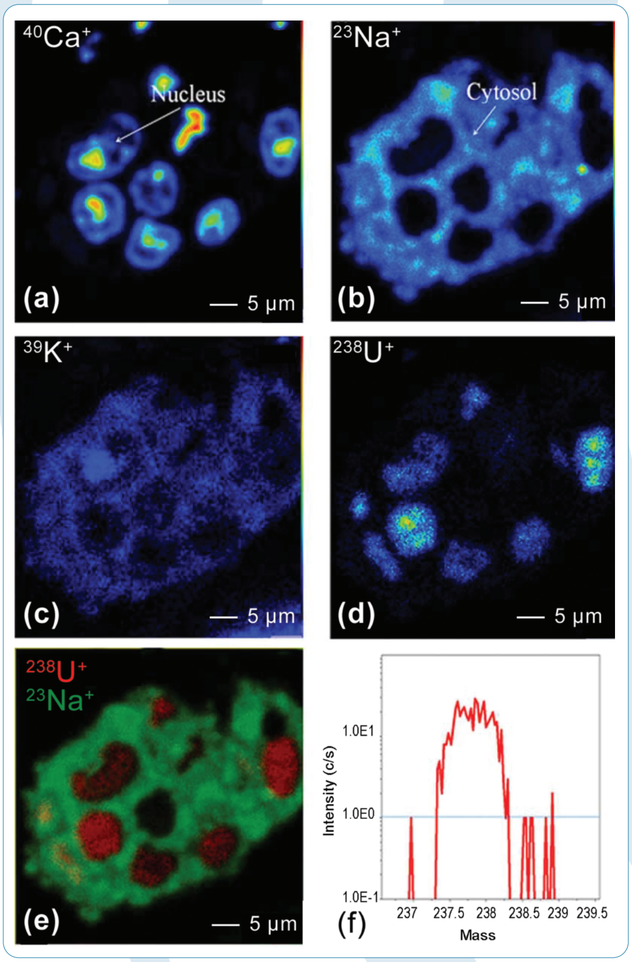

Figure 2: Uranium distribution inside the HepG2 cells after exposure to 50 µM of uranyl nitrate for 30 min, chemical preparation. (a) $^{40}Ca^+$, (b) $^{23}Na^+$, (c) $^{39}K^+$, (d) $^{238}U^+$, (e) superposition of $^{238}U^+$(red) and $^{23}Na^+$(green), (f) $^{238}U^+$ mass spectrum. Field of view: 50 x 50 µm².

Data collected on IMS 7f at IRSN Fontenay-aux-Roses (France). Adapted from D. Suhard et al., Microsc Res Tech. (2018) DOI: 10.1002/jemt.23047.

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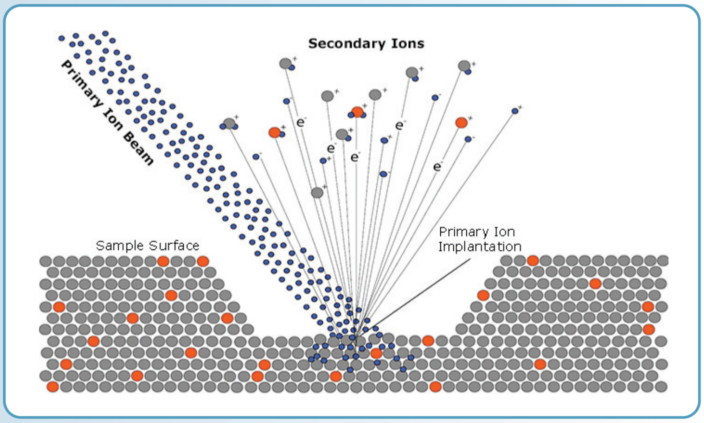
The technology behind



Dynamic SIMS

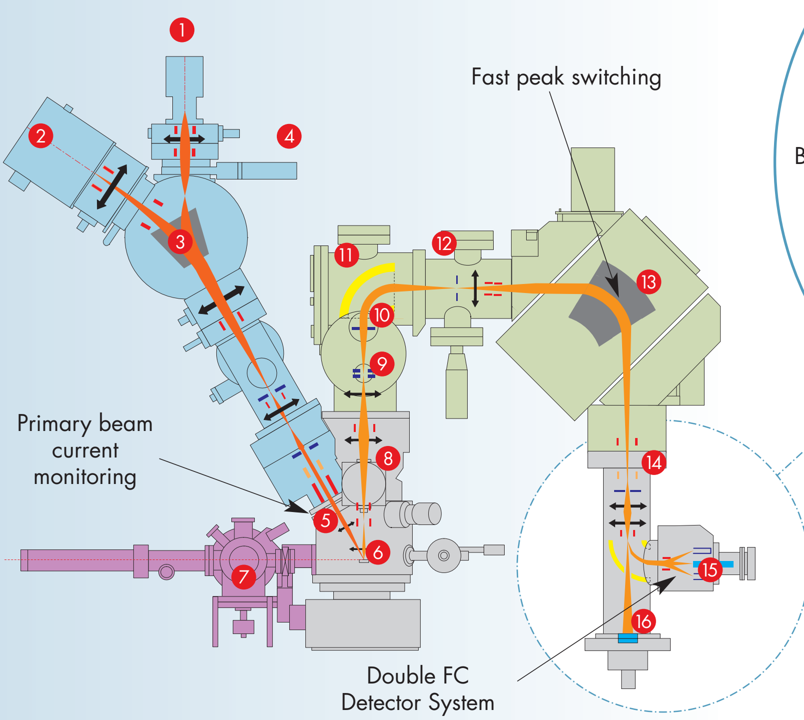
When a solid sample is sputtered by primary ions of few keV energy, a fraction of the particles emitted from the target is ionized. Secondary Ion Mass Spectrometry consists of analyzing these secondary ions with a mass spectrometer.

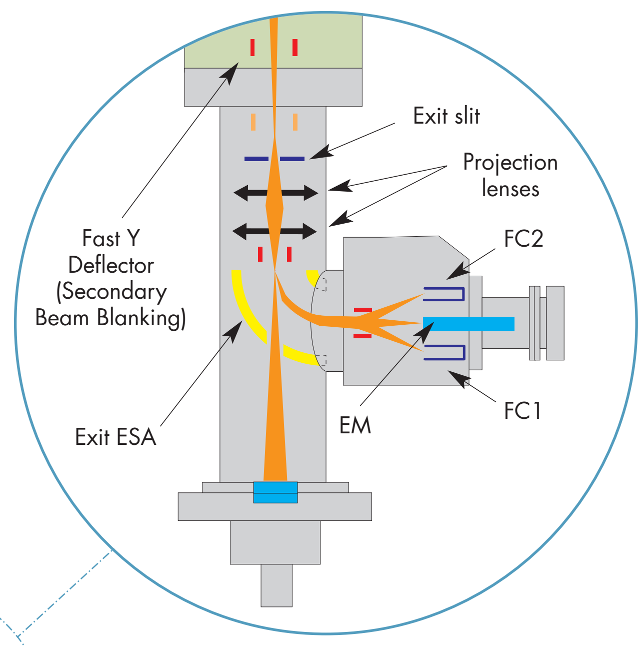
The SIMS technique is "destructive" by its nature (sputtering of material). It can be applied to any type of flat, solid material that can be kept under vacuum.

In dynamic SIMS, bulk composition and in-depth distribution of trace elements are investigated with a depth resolution ranging from sub-nm to tens of nm. SIMS is recognized as the most sensitive elemental and isotopic surface analysis technique.

CAMECA IMS 7f-GEO

The IMS 7f-GEO is a mono-collection SIMS model that combines the well-proven features of the IMS 7f with a specific detection system including two Faraday cups and one Electron Multiplier.





1 Microbeam Cesium ion source
2 Duoplasmatron ion source
3 Primary Beam Mass Filter (PBMF)
4 Cesium source isolation option
5 Primary Faraday cup Motor driven primary column aperture
6 Sample (-10kV to +10kV) (Z axis in option)
7 UHV airlock system (Sample storage chamber in option)
8 Normal incidence Electron Gun (NEG)
9 Motor driven contrast aperture and entrance slit
10 Motor driven field aperture
11 Electrostatic Analyzer (ESA)
12 Motor driven energy slit
13 Fast laminated magnet
14 Motor driven exit slit
15 Electron Multiplier and double FC detectors
16 Ion image detector

For more information please visit www.cameca.com/products/sims/ims7f-geo

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