Development of the unique UHV instrument allowing correlation FIB-SEM-SIMS analysis

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Benefiting from its extensive knowledge and its in-depth expertise in dual beam FIB/SEM (Focused Ion Beam/ Scanning Electron Microscope) systems and UHV (Ultra High Vacuum) environment, Orsay Physics has developed a convenient versatile and customizable instrument called NanoSpace allowing correlation of FIB-SEM with SIMS (Secondary Ions Mass Spectrometry) analyses. The SIMS is a label-free technique that not only reveals the chemical composition of a biological sample providing an excellent metabolite and lipid detection, but also cell phenotype discrimination.

The SIMS analysis is performed by the combination of a new secondary ion extraction column and an OTOF (Orthogonal Time Of Flight) detector which has the advantage of a simultaneous detection of all the masses and a dynamic range of 10^{6} - 10^{7} . Both have been completely optimized in order to enhance the collection of the secondary ions and increase the mass resolution (M/ Δ M) of above 5,000. In addition, as the NanoSpace is working in UHV, surface analysis and imaging are all the more reliable in a contaminant-free environment (pressure condition below 5.10^{-10} mbar inside the chamber). A very wide range of ion species can be chosen as the primary ion beam according to the user needs, including Xe⁺, Ar⁺, O²⁺, Si⁺, Au⁺, and even gold clusters. Finally, the SEM instrument allows to obtain high resolution imaging (<2 nm).

The development of this new tool is an instrument of interest in biology to obtain both *in situ* chemical analysis and 3D tomography of a biological sample at the nanometric scale. The sample preparation could require a washing using a volatile salt solution to maintain the osmotic pressure, *e.g.* ammonium formate, and then a freeze drying in liquid propane or nitrogen or high pressure freezing. Thus, no special sample preparation technique (dehydration, fixation, etc...) are necessary making the NanoSpace an easy and versatile instrument.

<u>Keywords</u>: SIMS, FIB, SEM, correlative analyses, *in-situ* analyses, Cryo mode